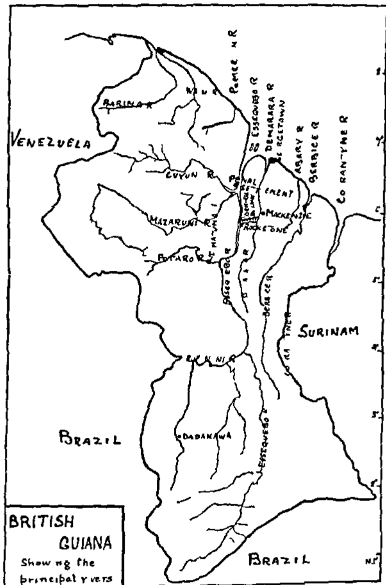
MALARIAL NEPHRITIS


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MALARIAL NEPHRITIS

EPIDEMIOLOGICAL AND CLINICAL NOTES ON MALARIA BLACKWATER FEVER ALBUMINURIA AND NEPHRITIS IN THE INTERIOR OF BRITISH GUIANA BASED ON SEVEN YEARS CONTINUAL OBSERVATION

By

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WITH 17 ILLUSTRATIONS



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PREFACE

I WISH to acknowledge my indebtedness to the late Mr R H Carr Managing Director and to Mr F B Henderson Manager of The Demerara Bauxite Co Ltd for the ample opportunities and means which have been given me for carrying out my researches to Dr P J Kelly Surgeon General of British Guiana for supplying most of the official statistical data to Dr P Manson Bahr *D.S O* and Dr J Tertius Clark for valuable bibliographical references to Dr A Balfour C B C M G and Dr J Gordon Thomson for kindly reading through my manuscript

I also wish to thank Dr J F C Haslam *M C* for his invaluable assistance and for kindly correcting the proofs of this book for the press

GEORGE GIGLIOLI

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PART III

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INTRODUCTION

MALARIAL nephritis is a very frequent condition in British Guiana

Apart from the local interest which the observations and conclusions contained in this book may have in regard to the solution of one of the most important health problems of this Colony I believe that this work may attract attention to renal disease as a consequence of chronic malaria particularly of the quartan type in many other countries where similar ecological and epidemiological conditions prevail

As regards the study of the pathology of malaria on the one hand and of renal diseases on the other the need of well documented observations on malarial nephritis has long been felt

The observations and statistics given by different authors on the incidence and characters of albuminuria and nephritis in malaria are most remarkably varied and often contradictory the clinical and anatomical pictures described are equally different

In text books on renal pathology malaria is usually given as an important etiological factor in relation to Bright s disease while in many of the most authoritative works on malaria the rarity of kidney complications is emphasised

From a careful study of the literature and from personal clinical and epidemiological observations carried out under exceptionally favourable conditions in British Guiana I have formed the opinion that most of the discrepancies noted in the observations reported by the various authors are justified and rather than excluding tend to *confirm* the etiological relation between malaria and kidney disease

Malaria produces nephritis only if special conditions

prevail These concern the *species of the infecting malarial parasite* the *intensity* of the infection and its *duration* and *persistence* The clinical symptomatology and the type of the anatomical lesions are equally governed by these factors

As the endemiology and epidemiology of malaria vary within wide limits under the influence of the infinite number of factors affecting the parasite its insect vector and its human host in the same way the renal diseases which malaria may determine are liable to great variation as regards their incidence clinical character and anatomical type

I wish to emphasise that the conditions which favour malarial nephritis are not in the nature of contingencies bringing about a complication of a secondary or accidental character they are conditions which influence directly and exclusively the epidemic regime of malaria

It is for these reasons that the present booklet though concerned essentially with the study of malarial nephritis deals extensively with the epidemiology of malaria and black water fever in British Guiana Without such a preliminary the conditions which cause malarial nephritis to prevail as one of the commonest and most fatal diseases of the Colony could scarcely be understood or appreciated

MALARIAL NEPHRITIS

PART I

EPIDEMIOLOGY OF MALARIA IN THE INTERIOR OF BRITISH GUIANA

EPIDEMIOLOGY OF MALARIA ON THE TIDAL RIVERS

Geographical

BRITISH GUIANA lies between the 1st and 9th degrees of North latitude

Relatively to its physical characteristics the country may be roughly divided into the following four zones running more or less parallel to the coast line —

The costal alluvial plain

The sand hill zone

The mountainous zone

The savannahs of the far interior

Towards the western frontier in the North West District the distinction between these zones is less apparent as the mountains rise at a very short distance from the coast but as one proceeds eastwards towards the Surinam boundary the zones broaden out progressively and are well defined They are particularly evident on the Demerara and Berbice rivers

The coastal plains are formed by alluvial and detrital deposits they extend inland to a breadth of 10 to 50 miles from the coast and are in part below high tide level They are extensively cultivated and an elaborate system of

dams drains sluices back dams and pumping stations defends them from high tides and floods and provides *in part* for the disposal of drainage water In Berbice the plantation belt is succeeded by very extensive swampy savannahs used as pasture lands and for the cultivation of rice

At a variable distance from the coast—15 to 20 miles in the west and 40 to 50 miles in the eastern part of the Colony—forest covered sand dunes and sand hills make their appearance gradually increasing in height as one proceeds inland

The first low mountain ranges rise from 40 to 120 miles inland rocky dams obstruct the valleys causing the formation of rapids and falls and the rivers abruptly acquire a torrential or flood character

The waters of the Caribbean Sea which along this part of the South American coast are very muddy flow up the rivers and creeks with the powerful rising tides for a distance of 25 *miles and more All the surface waters of the coastal* alluvial plain are more or less muddy and are frequently brackish The level of the rivers here is only influenced by tidal variations the system of sea defences though much improved during recent years is as yet quite inadequate to cope with the elimination of flood water during the heavy rains Miles and miles of country are submerged at these periods often in immediate proximity to towns and villages

Throughout the sand hill zone the rivers maintain their tidal character the waters are brown *vegetable stained* but limpid and very soft The mangroves so characteristic of the coastlands disappear and are substituted by a thick growth of giant arums (*Caladium arborescens*) which fringe the low forest clad banks The ground is nowhere visible except where axe and cutlass have opened a way

The river banks are only a few inches above high tide level and are formed by alluvial mud flats which extend for a considerable but variable distance to the foot of the hills

They present some peculiar characteristics of considerable interest to the malariologist

The river bank proper is fairly high but falls gradually away on either hand *Extensive permanent swamps formed* by tide rain and seepage waters lie along the foot of the hills running parallel to the river banks

Thick high forest characterised by the prevalence of the graceful slender nibong palm covers these swamps Our photographs and Fig 1 will give a clear idea of their

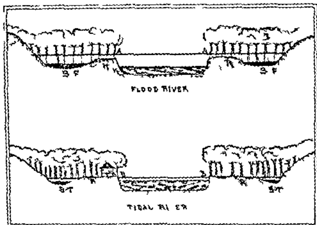


Fig 1 —Showing [illegible]

position in relation to the inhabited portions of the river banks

The distance which separates the river banks from the foot of the hills varies over an average of roughly some 300 yards Towards the interior the hills become high and the valleys narrower and the extent of the mud flats becomes much reduced On this impermeable soil every depression *holds water during the rains and the thick overhanging* vegetation prevents it from evaporating rapidly

Above the first rapids the general characteristics of the rivers are similar but the tidal is substituted by the flood *regime* The valleys are periodically swept by mighty floods regulated by the rainfall on the upper reaches of the rivers

The savannahs of the far interior are extensive rolling grassy plains situated at a considerable elevation above the sea They are intersected by numerous rivers belonging both to the Essequebo and the Amazon systems ponds and lakes abound and during the summer rains very extensive floods occur

The towns and larger villages are situated in the coastal belt mainly between the mouth of the Essequebo river and that of the Courantyne This area accounts for eight tenths of the total population of the Colony

The rapids and falls have proved an insurmountable obstacle to the progress of colonisation as the rivers are the only ways of communication With a few negligible exceptions permanent settlements are not to be found above the first rapids on any of the Guiana rivers

On the other hand a considerable population has settled along the tidal tract of these rivers mainly on the Demerara Berbice and Essequebo and to a lesser extent on the Waini Moruca Pomeroon Canje and Courantyne

We have described the general topographical characteristics of these rivers which also share very much the same general meteorological climatic and ethnographical conditions

At the present day the study of malaria in the inhabited portion of the interior on the tidal rivers is of considerable importance Malaria accounts for an enormous amount of disability and a high mortality amongst the population of these regions and is responsible for a large proportion of the sickness seen on the coast among men who have been temporarily working in the interior It is therefore a serious obstacle to be carefully considered in the undertaking of any scheme of colonisation or exploitation of the interior

Meteorological

Rainfall.—Fig. gives the average rainfall as registered by the Meteorological Station at the Government Botanical Gardens in Georgetown during the period 1907 to 1926. The annual rainfall averages 91.65 inches (1880 to 1929).

We note two seasons of relatively scarce rainfall corresponding to the months February, March, April and September, October, November respectively. The rains are abundant in January, May, June, July and December.

Comparing the Georgetown average rainfall curve with those of two other coastal meteorological stations situated

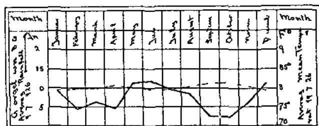


FIG. —Monthly average rainfall and average mean temperature at Georgetown

at New Amsterdam in Berbice and Suddie in Essequebo (twenty years' record) we find that their course is parallel.

In Berbice the rainfall appears to be uniformly lower with an average total yearly precipitation of 74.94 inches (1907 to 1926).

At the Penal Settlement, forty-two miles south of the coastline on the Essequebo in hilly country at an elevation of 25 feet, the average rainfall during the summer months (May to September) is considerably higher than on the coast. The yearly average is of 103.67 inches (1906 to 19 5).

At Mackenzie on the Demerara river sixty-five miles inland, the annual precipitation is somewhat higher than on

the coast the curve has a similar character keeping above 6 inches during the months of September October and November The average yearly precipitation during seven years observation was 103 17 inches

The rainfall in the mountainous districts of the interior as on the Potaro and upper Mazaruni rivers is extremely heavy averaging roughly from 130 to 140 inches per annum During the wet seasons May to August and again in December and January the rains are extremely

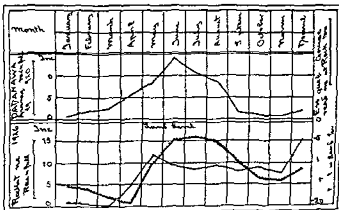


Fig 3—Average monthly rainfall at Dadanawa (plain land savannah) and rainfall and river level at P k ton (mid F eq h)

violent and monthly precipitations of 30 inches are not exceptional

In the far interior rainfall conditions are very different At Dadanawa situated at 320 miles from the coast on the Rupununi river the average yearly rainfall over a period of nine years was 58 51 inches There is only one rainy season from May to September during the rest of the year the average monthly rainfall does not exceed 2 inches The seasons are very well marked (Fig 3)

It is in the great savannahs of the far interior that the

large rivers have their origin and this clean cut *régime* of the rainfall regulates the periodic pulse of the great floods

The study of the average curves is useful as a means of determining the approximate yearly rainfall *régime* but variations from the average in Guiana are far more the rule than the exception Taking for instance the maximum and minimum monthly rainfalls registered in Georgetown during the past twenty years we find the following striking figures

Month		Av.	Max.	Min.
	January	[illegible] 8	18 18	1 93
Maximum	February	[illegible]	13 38	0 45
Minimum	March	6 31	[illegible]	0 28
and	April	4 81	10 [illegible]	0 [illegible]
Average	May	11 [illegible]	3 38	[illegible]
Monthly	June	11 80	[illegible]	[illegible]
rainfall	July	[illegible]	11 6	3 [illegible]
190[illegible] [illegible]	August	[illegible] 44	14 [illegible]	3 [illegible]
Government	September	3 08	6 8[illegible]	0 10
Botanical	October	3 01	8 9	0 1[illegible]
Gardens	November	[illegible]	[illegible]	0
	December	11 [illegible]	0 0[illegible]	41

Fig 4 shows the monthly rainfall curve registered at Mackenzie during the period 19[illegible] to 192[illegible] It is a good illustration of the marked yearly irregularity It is from the study of these seasonal irregularities that most light can be obtained as to the influence of meteorological factors on the epidemiology of diseases

Temperature —The climate of British Guiana is typically equatorial *i e* it is characterised by great uniformity throughout the year

The *average annual mean temperature registered* at Georgetown over a period of eighty years is 80 4 F The average monthly curve for the period 190[illegible] to 19[illegible] is shown

in Fig 2 The temperature is remarkably uniform the annual range not exceeding 3 The lowest mean temperature occurs in January with 78 8 F during the months of April May August September October and November the mean temperature is above 80 F In October it reaches its maximum with 81 5 F The mean diurnal range is 10 5 F The average minimum temperature oscillates between 74 and 76 only exceptionally falling below the former figure

At New Amsterdam in Berbice (twenty years average) the temperature is uniformly slightly higher with a yearly average of 80 9 The mean daily range is more marked with 13 5 F

At Mackenzie over a period of seven years observation (1922 to 1928) we had the following figures —

Average annual mean temperature	81 11 F
Average annual maximum temperature	89 12 F
Average annual minimum temperature	73 10 F
Mean diurnal range	16 02 F

The mean temperature curve keeps below 80 F during the first three months of the year It then progressively *rises to find its maximum in* September (83 54) October 83 56) November (83 34) It again falls in December The minimum temperature curve tends to keep below 74 F not rarely falling below 70 F The mean diurnal range is considerable averaging 16 02 F

In comparison with the coastal figures we find —

A slightly higher annual mean temperature a considerably lower average minimum temperature and a much wider mean diurnal range In Fig 4 the monthly mean maximum and minimum temperature curves are given for the years 1923 to 1928

Winds —The north east trade winds which blow on the coast during the whole year are much less perceptible in the forest areas of the interior During the dry weather on the

Rupununi savannahs a strong wind blows constantly from the north east

Moisture—The only existing records are those from the coastal meteorological stations. No regular registration has been carried out in the interior where conditions are quite different. The existing records are therefore of little use for our purpose

Ethnographical

The history of British Guiana is the history of its plantations coffee cocoa cotton sugar

The population of British Guiana as found to day is the result of various labour immigration schemes dating back to the early *times of European occupation* the importation of efficient agricultural labour still represents one of the most important and difficult of the Colony's problems

The importation of negroes as slaves from the West Coast of Africa continued up to 1807. In 1834 emancipation was proclaimed. The freed negroes rapidly abandoned the plantations and the importation of new labour became an urgent necessity

Between 1835 and 1882 39 645 Portuguese came to the Colony from Madeira and 14 000 Chinese immigrated between the years 1853 and 187 The East Indian immigration *began in 1838 and continued up to 1917* totalling the important figure of 39 979. These immigrants hailing from such widely different countries came to Guiana to work *the plantations and settled* and learned to live in the new country where and as their work required

The fertile swampy alluvial coastal plain prevalently below high tide level and the low mud flats bordering the tidal rivers became their home. It may well be said that the newcomers to Guiana have been systematically trained to live in the swampy lowlands

No benefit has been gained by contact with the aboriginals of the land. The *Indians either retired before* the invaders

or rapidly merged by intermarriage into the new population *renouncing the customs and traditions and the experience* gained by centuries of strife which had enabled them to thrive in the country

At the end of 1927 the population of British Guiana was estimated at 308 473 with the following racial distribution —

Europeans other than Portuguese	2 991
Portuguese	8 534
East Indians	128 069
Chinese	2 820
Aboriginal Indians	8 881
Negroes	12[illegible] 119
Mixed races	34 554
Other races	505

Over two thirds of the present population of the Colony are the result of immigration during the last ninety years

The population of the coastal area extending between the mouth of the Essequebo and Courantyne rivers is estimated at 245 818 souls *i e* eight tenths of the whole population

The inland river districts with which we are mainly concerned have an estimated aggregate population of 35 554 with the following distribution —

Lower Canje River	9 067
Upper Canje River	1 117
Berbice River	3 540
Demerara River	7 850
Lower Essequebo River	3 967
Upper Essequebo River	2 509
Upper Mazaruni River	1 211
Pomeroon and Moruca Rivers	6 293
Total	35 554

In reality the actual population of the river districts is

very considerably higher owing to the fluctuations caused by temporarily immigrated labourers from the coast and West Indian Islands In this connection the importance of health conditions in the river areas is much increased as there is little doubt that much sickness which is seen along the coast finds its origin in the interior

The typical population of the Guiana rivers is of mixed race with European South American Indian and Negro blood They are locally known as Bovianders (from the Dutch *boven lander*) Negroes are numerous but in majority only temporary labourers from the coast

On the upper reaches of the Berbice Mazaruni Canje Potaro and Essequebo there are no permanent inhabitants but only a fluctuating widely scattered and exclusively male population mainly constituted by negro pork knockers (diamond and gold diggers) and balata and timber workers The aboriginal Indians are estimated at from 9 000 to 0 000 Those found in the inhabited river areas are civilised and have acquired the customs of the Bovianders The primitive naked Indians are now only found in the far interior and are rapidly decreasing

On the Rupununi savannahs health conditions are reported to be excellent The Wapisiana and Macussi Indians are healthy sturdy races and are on the increase

Amongst the river population we find no knowledge custom or belief in regard to malaria fever or the means to avoid it Fever is not associated with swamps or any other particular outside condition It is regarded as an unavoidable routine in life and bile or biliousness as its cause

The medical knowledge of the mass of the population finds its source in the advertisements of patent drugs and cures with which the daily papers are well stocked Purges of all kinds and patent Bilious Pills and remedies are the only medicines sought There is an incredible prejudice against quinine and the drug is currently misused The doses

taken or administered are usually much too small and treatment is suspended as soon as the fever has abated The fear of its bringing on blackwater and abortion is most prevalent particularly amongst the better educated Paradoxical though it may seem in most cases education among the coloured natives only increases ignorance as it engenders a self assurance and an I know better attitude out of all proportion to their knowledge As regards medical knowledge among all classes the level is of the lowest It may here be noted that even among the dispensers to whom a large proportion of the population must look for medical treatment the conviction of the utility of their own practice is so poor that we find them resorting to calomel and patent pills of all descriptions in preference to quinine when treating themselves or their families for malaria

Excessive elimination of bile pigments is one of the most characteristic features of malaria Obsolete hippocratic terminology still holds good in English medical jargon it is scarcely surprising if the native with his simple logic calls malaria *biliousness* and treats it accordingly And so untreated acute infections become chronic and chronic infections perpetuate themselves favoured if anything by the violent and repeated purging

Housing Conditions

The aboriginal Indians build their camps on high dry ground well above swamp level usually on the top of a sand hill (Fig 5) The rest of the population of Guiana 97 per cent of the total build their homesteads in the swamps below or only a few inches above high tide level (Fig 6 and 7)

Along the rivers the sand hills offer excellent healthy naturally drained well ventilated sites at a short distance from the water The bush on them is thin and once cleared is easily kept under control with a minimum of work In spite of these exceptionally favourable conditions



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all the settlements are situated on the low mud flats surrounded by high dense forests and permanent and seasonal swamps

The wooden houses are built on piles elevated 1 to 8 feet from the ground They are palm thatched or wood shingled divided into two or three small rooms by low partitions The whole family crowds into these parents and children sleeping together Mosquito nets are a rare luxury



FIG — A street of the village of Christianburg built feet above the level of the surrounding ground in order to render access possible during the rains and spring tides Note the uninhabited *sand hills in the background*

Labourers are usually housed in plain palm thatched sheds under which they sling their hammocks

The houses may be surrounded by a small clearing or pasture or by a provision field or farm

The people are mainly engaged in timber work and in cultivating the small farms for the use of their households

If one excludes the villages of Christianburg, Wismar and Mackenzie which have developed under the impulse of the bauxite industry on all the Guiana rivers the population

is sparsely distributed the houses are isolated each family with its dependents keeping to itself The village population is multicoloured formed mainly by temporary immigrants from the coast there is a marked prevalence of the negro element

The isolated river settlements on the contrary are inhabited almot entirely by Bovianders and aborigines

Dietary

The study of the native dietary among the various races in British Guiana has not yet been taken up It will be enough here to mention the customary dietary of the river population

The greater part of the food is self produced or self procured the farms supply cassava and a variety of other starchy tubers and vegetables uch as yams eddoes tannias and sweet potatoes corn bananas plantains and peppers From the rivers fish is easily obtainable and used fresh pickled or smoke dried Game is scarce From the stores the supplies currently bought are flour ice and sugar Tinned food salt fish and meat are rarely used by the Indians and coloured settlers more so by the negroes employed as temporary workers on timber grants or other jobs where there is no opportunity for procuring fresh fish or game

For condiments the grea e of fish or meat when available is the only grease used by the poorer those who can afford it use salt pork The poisonous juice expressed from grated cassava is boiled after sedimentation of the starch and used as it is (cassareep) or it may be stored and seasoned with fresh red peppers and salt fresh meat and fish and more cassareep are added at intervals whenever available and the mixture boiled and re boiled at every meal This is the well known pepper pot which is kept going for days new ingredients being continually added

Cassava or plantains form the main base of each of the

three more or less equal meals which are taken throughout the day

This dietary would appear fairly well balanced though tending to a marked starchy excess with relative deficiency of fats The point to be emphasised is the *self produced* and *self procured* character of the foodstuffs Any interference with the somewhat precarious supply of fish or game will tend to accentuate the already noted starchy excess of the dietary On the other hand any influence hindering the proper growth of the crops or the cultivation of the farms will lead to poverty and starvation The population is very poor and especially in times of scarcity the purchase of flour or other foods is impossible

Anopheles Mosquitoes

Further research on this subject is required *A tarsimaculata* a well known malaria carrier in Panama and the West Indian islands is the common vector along the coast (Bodkin 1921)

As in Panama it is found to have a preference for slightly brackish waters It breeds in open country in ill kept drains and trenches which are choked with vegetable growth forming small pools inaccessible to fish and in small hollows where the bottom is impermeable and which are partly protected from the influence of the sun and wind by coarse grass and weeds The sodium chloride contents of the waters harbouring *A tarsimaculata* ranged in Georgetown from 4 9 to 1 378 7 per 10 000 parts (report of the C M O H for 1926) Leprince reports from Panama that Catun lake became a dangerous intensive breeding ground for this species as soon as sea water was admitted and the lake from sweet became brackish

In Surinam Bonne and Bonne Wepster found *A tarsimaculata* to be the main carrier on the coast where it was commonly found in the houses of the plantation coolies In the interior they found this species represented by a

variety with slightly different morphological characters and absolutely different biting habits it was never found in houses being an exclusively bush mosquito apparently with no practical importance concerning the spread of malaria

In the interior of British Guiana *A tarsimaculata* is rare I have never caught it in houses On two occasions during 1929 I found it breeding in open sun exposed puddles in localities which had been cleared of bush at Mackenzie on the Demerara river

The main malaria vector in the interior of the Colony is *A argyritarsis* usually regarded as an unimportant malaria carrier Bodkin in 1921 was the first to recognise this species in the interior at Rockstone and in the Potaro district During the summer of 1929 over 3 000 adult anopheles were collected on the mid Demerara river all identified as *A argyritarsis* this species only was collected on the mid Essequebo and Potaro Such findings confirmed Bodkin s observations and my own findings of the preceding six years of which systematic records were not kept

No figures are yet available concerning the natural rate of infection of *A argyritarsis* caught in native houses or on the rate of infection amongst laboratory bred mosquitoes fed on malaria patients

In Surinam with general conditions very similar to those of British Guiana Bonne and Bonne Wepster failed to find *A argyritarsis* along the coast it was common in the interior it showed a marked tendency to congregate in houses its distribution corresponded to the worst malaria localities in the Colony This species was found infected in nature with oocysts of all three species of malarial para sites and these authors regard it as probably a better intermediate host for the æstivo autumnal parasite than *A tarsimaculata*

A argyritarsis can be found in the adult stage at all times of the year but in varying numbers It is most easily

caught in houses where it sometimes congregates in enormous numbers These mosquitoes are attracted by light and I have seen them fly across the Demerara river to the strong electric lights on the landing stages at Mackenzie They abound and are very active during the hot months following the summer rains from July to November With the



Fig 8 —T lal and seep e swamp t Mackenz situated on th mud flat at the b e of the san l hill The hou es in th left backgrou id are placed on the river bank the hi h tide w ters nter the s amp th ou h a sm ll creek This swamp wa in origin covered by thick for t an l was a prod icti e breedin ite for *A argyr tarsis* this mo quito disappeared after th bush was l are l w tho t othe wi e alterin the water con lit on

onset of the winter rains they rapidly decrease and become much less active

Bonne and Bonne Wepster in Surinam experienced some difficulty in locating the breeding sites of this species they finally found them in swampy places showing an abundant growth of green algæ

It has been shown how abundant and varied are the sur face waters on the low banks of the rivers the tidal swamps

with their bi-quotidian flushing and abundance of small fish are not favourable sites for the breeding of mosquitoes. Larvae are frequently found safely hidden in the innumerable small puddles which persist from one tide to the other amongst the labyrinth of buttress roots of the great mora and other forest trees. The ideal breeding places are formed by seepage and rain swamp, as they are devoid of fish and persist for many weeks during and after the rains. The



Fig. 10. — Pools of swamp left by the falling flood of the [illegible]

holes and furrows left by the falling away of decaying roots and stumps form the most typical breeding sites. The peculiar configuration of the low mud flats which constitute the river banks and on which the settlements are situated should be kept in mind (Figs. 1, 8 and 9).

Amongst the man-made breeding places the swampy hoof-trodden pastures and the native provision fields merit special attention. When the bush is felled and burnt as a preliminary for the planting of a provision field or farm

many of the tree stumps and roots burn for a depth of 1 or 2 feet below ground level The fields are thus riddled with these deep narrow holes in which rainwater is caught and stored for weeks owing to the impermeable nature of the soil and scanty evaporation through the narrow orifice These are soon covered by weeds and crops becoming ideal and dangerous breeding sites in the immediate neighbourhood of habitations

Protection of the water collections from direct exposure *to the sun s rays seems to be an important condition for the* breeding of *A argyritarsis* I have never found its larvæ in the grassy puddles of the open pastures where Culex larvæ abound and *A tarsimaculata* is sometimes found The question of bush and bush clearing is therefore one of first importance as regards this species On the swampy mud flats which border the rivers vegetation is very thick powerful and encroaching

The breeding season of *A argyritarsis* is well defined and begins towards the end of the summer rains when the temperature has risen well over 80 F and continues throughout the hot weather (August September October and November) as long as favourable surface water conditions persist The heavy rains in December and January are without doubt unfavourable to the adult mosquitoes a large number of them are killed off while the lowered mean temperature is not favourable to breeding The autumn rains in spite of *extensive flooding are not followed* by an increase in the number of anopheles and larvæ are not to be found in spite of the fact that surface water conditions appear just as favourable as during *the summer rains*

During February March and April adult anopheles are still found in considerable numbers but appear to be much less active than in the hot *weather in some instances* they appear to be in an actual quiescent or hibernating condition

On one occasion in April 19_8 I slept with a friend for

four nights in a small open rest house on the Abarry river at about forty miles from the coast. The surrounding country was open swampy savannah and cattle pasture with high grass and clumps of bush; we were never disturbed by mosquitoes, which on previous occasions had been very plentiful. On the second day of our stay I was surprised to find that numerous anopheles were resting in the darker and more sheltered corners of the house. I collected about sixty specimens; all were *A. argyritarsis* and not one appeared to have fed on blood recently. Though systematic search was made during the following days I found no more. Evidently these insects had been in the house for a considerable time in a quiescent condition, as no attempt to feed on us was made and no more entered the house during the subsequent days of our stay. Unfortunately I did not have the means of examining these mosquitoes for the presence of fat bodies.

It appears likely that the link between one breeding season and the other, from November to June, is made by these adult females and not by means of larvae or eggs, as occurs in temperate climates according to some authorities. I have seen anopheles appear early and in unusually large numbers during the rains following prolonged intense droughts which had parched the country during the winter months (1926). Excessive heat and prolonged drought could not be a favourable condition for the mass survival of eggs or larvae; it would, on the contrary, be very favourable for the survival of large numbers of adult insects, which would thus be spared the deleterious action of the violent autumn and winter rains.

On the savannahs of the Rupununi mosquitoes occur in very large numbers from July to October. I have not been able to ascertain whether anopheles are found. The insects are reported to feed mainly on the cattle and horses and to have a limited range of flight. A clearing of 150 feet around the ranches is considered sufficient to avoid them.

Malaria Parasites

Out of 3 112 blood films examined for malaria parasites (thin films) during the period May 1926 to December 1928 1 247 were returned as positive (40 per cent)

There is a very considerable number of cases which though undoubtedly malarial give a negative blood examination This is due mainly to the following facts (*a*) Most of the labourers come to hospital after having received preliminary treatment at our dispensaries quinine has therefore been already administered at the time of the blood examination (*b*) Our laboratory routine consists in the examination of a single thin blood film many slight infections *therefore escape detection*

The 1 247 positive blood examinations can be classified as follows —

P vivax rings	850
P vivax trophozoites	134
P vivax gametes	32
	1 016
P falciparum rings	175
P falciparum crescents	21
	196
P malaria	35
Double infections *P v —P f*	52
P f—P m	2
	54

From these figures it appears that benign tertian accounted for 81 4 per cent of the total malignant tertian for 15 7 per cent *quartan for 2 9 per cent*

If the relative monthly incidence of *P vivax* and *P*

falciparum infections is *considered* we find that the subtertian parasite is common during the *late* summer and autumn months. This infection becomes therefore more frequent when the meteorological conditions are such as to prolong the active malarial season into the autumn (192[illegible]).

The remarkable rarity with which crescents are found is worthy of *note*—only in twenty one instances in 1[illegible]4[illegible] positive bloods.

The quartan parasite appears from our statistics as the least common. Quartan infections are in reality quite common particularly during the autumn and winter months but owing *to the* mildness of the disease such cases are not frequently seen in hospital.

In November 19[illegible]6 during a house to house examination along the whole length of the inhabited portion of the *Demerara river* which *I carried out in* association with Dr Ozzard we were struck by the frequency of *P. malariæ* in the blood films we collected. *In* 1929 I carried out a similar survey on a smaller scale with much the same results. There is no doubt in conclusion *that* quartan malaria is very much commoner than our figures would imply. On the other hand it is practically impossible to distinguish *P. vivax* from *P. malariæ* when only ring forms are found in a film. In routine work large rings are registered as *P. vivax*. *P. malariæ* is recognised only when trophozoites, rosettes or gametes are found. For exact work it would be necessary to re-examine bloods showing large ring infections after *an* interval of twenty four hours.

The results of these *observations* appear in patent opposition to what one reads in the report of *the* Departmental Medical Conference held in Georgetown, British Guiana, on malaria in 19[illegible] (page 3, paragraph 18).

"In the opinion of *the* Government bacteriologist the frequency of *malignant* tertian was considerably greater than the other *types*. That experience however might be due to the effect of the greater severity of malignant tertian

infection resulting in more patients of this type being sent to hospital for treatment than in the case of the other types

The benign tertian form is most commonly found in the coastal areas

The quartan form is found but by no means commonly

As regards river bank areas the most usual type was the malignant and this also applied to the hinterland areas

Seasonal Periodicity of Malaria on the Tidal Rivers of British Guiana

Malaria is hyper endemic in the tidal portion of the Guiana rivers

In 1926 during a house to house survey extending throughout the whole of the inhabited portion of the Demerara river Dr Ozzard and I found enlarged palpable spleens in approximately 100 per cent of the Boviander children below fifteen years of age

In 1929 in a similar survey extending over a stretch of twenty miles above Christianburg on the Demerara river and covering forty Boviander and aboriginal Indian children I found a spleen rate of 76 1 per cent most of the spleens were very large

In the village of Mackenzie in which the negro element prevails the spleen rate among fifty four children ranging from one to fifteen years of age was 26 per cent as follows —

Race	Number Examined	Enlarged Spleen	Per cent
Negro	31	5	*16 per cent*
East Indian	2	1	—
Mixed	21	8	38 per cent

These figures are insufficient for reliable conclusions For the collection of satisfactory data much travelling and time would be required as children are scarce on the

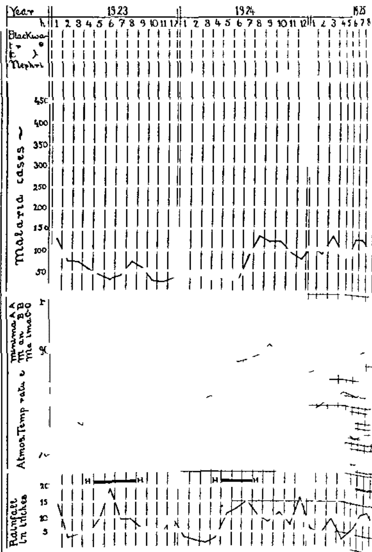
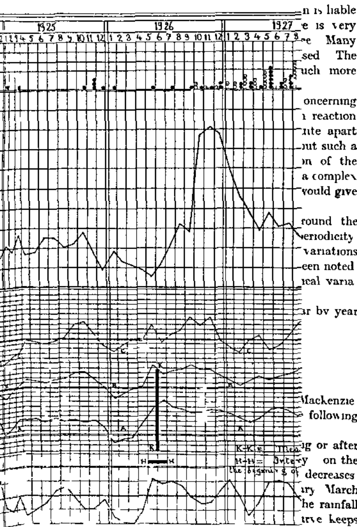


Fig 4.—Graphs of a r al temp



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(3) The malaria curve keeps low during May and June in spite of high rainfall It rises constantly towards the end or after the summer rains after an interval of variable duration (Fig 4 H H)

(4) The duration of the interval between the onset of the summer rains and the rise in the malaria curve varies in inverse proportion to the height of the mean temperature curve (Fig 4 ratio between H H and K K)

(5) The onset of the December rains with the synchronous fall of the mean temperature marks the fall of the malaria curve

If we consider the rainfall temperature and malaria curves in each individual year other interesting points can be noted —

1923 —METEOROLOGICAL CHARACTERISTICS

(1) High rainfall in January (14 05 inches)
(2) Rainfall during February March April and July August September October November average
(3) Summer rains last only for May and June
(4) Aggregate rainfall for the May to October period 58 14 inches
(5) For the same period the average mean temperature is 80 60 F

MALARIA

(1) The malaria curve is low throughout the year and only a very small summer rise is registered during August and September
(2) The interval between the rise in the rainfall curve (May) and the rise in the malaria curve (August) is of four months During the interval the mean temperature is only 79 68 F

GENERAL MORTALITY

Mortality from all causes was low and remarkably uniform throughout the year

1924—METEOROLOGICAL CHARACTERISTICS

(1) Low rainfall in January (3 49 inches)
(2) Rainfall in February March April below average Rainfall during July August September October and November above average
(3) Summer rains persist from May to October
(4) Aggregate rainfall during the May to October period 71 46 inches
(5) For the same period the average mean temperature is 80 60 F The average minimum temperature is 7[illegible] 61 F

MALARIA

(1) The malaria curve is very low up to June It rises rapidly in July remains high to the end of the year
(2) The interval between the rise of the rainfall curve (May) and the rise of the malaria curve (July) is of three months During this interval the average mean temperature is low (80 04 F)

GENERAL MORTALITY

The number of deaths registered in the district showed a distinct rise corresponding to the rise in the malaria curve

The years 19[illegible]5 and 1927 as post epidemic years will be considered separately under the heading of relapses

1926—METEOROLOGICAL CHARACTERISTICS

(1) Exceptionally low rainfall in January (2 64 inches)
(2) Rainfall during February March April far below average (aggregate 5 41 inches) Rainfall during July August September October above average
(3) Summer rains persist from May to September
(4) The aggregate rainfall during the period May to October is 70 33 inches
(5) For the same period the average mean temperature

is 83 82 F The average minimum temperature is 75 66 F

MALARIA

(1) The malaria curve is very low up to May it rises rapidly from June to November

(2) The interval between the rise in the rainfall curve (May) and the *rise in the malaria curve (June)* is two months During this interval the average mean temperature is 83 70 F

GENERAL MORTALITY

The number of deaths registered during the last five months of the year in correspondence to the rise in the malaria curve was four times larger than the number registered in the preceding three years [1]

1928 —METEOROLOGICAL CHARACTERISTICS

(1) Rainfall in January average

(2) Rainfall during February March April and July August September October average

(3) Summer rainfall scarce May and June

(4) Aggregate rainfall for the May to October period 49 29 inches

(5) For the same period the mean temperature is 82 58 F

MALARIA

(1) The malaria curve is still influenced by the 1926 epidemic It follows a parallel course to the rainfall curve up to May It then rises progressively during the summer

[1] During th period Sept mber 19 6 to August 19 a serious outbreak of *Par typh l C* occurred in the di trict with a high mortality (3 per cent in ou hospital) It is probabl that a very considerable number of e which did not receive ho pital tr atment and died w registered as malari In 135 cases seen in our hospital J per c nt presented a on omitant m l ria infect on On the apparent epidem ological relation b tween *P ratyph d C* and m la ia I have rep rted els where

(2) The interval between the rise of the rainfall curve (May) and the rise in the malaria curve is not apparent owing to the synchronous rise of the two curves during May (see below under Relapses) It can be estimated at one month as in June the malaria curve continues to rise in spite of the rapid decline of the rainfall

General Mortality

The number of deaths registered has fallen to half the number registered during the two preceding years

From the Registrar General s returns showing the number of deaths registered month by month in the various districts one notes an identical increase in the number of deaths starting from October 1926 in all the tidal river districts This increase is least noticeable in the Pomeroon district where it amounted to 19 7 per cent on the average mortality of the preceding four years in the Mara and upper Berbice district the increase was of 48 8 per cent on the Moruca river it reached its maximum with 460 per cent

New and Chronic Malaria Infections Relapses Re infections and Super infections

In the present investigation it has not been possible to differentiate between new and chronic infections relapses re infections etc

The histories one can get from native patients are not reliable The spleen of a case who denies ever having had fever before will often be found to reach the pubis On the other hand patients who are known to suffer from frequent attacks of undoubted malaria may present on examination a perfectly indifferent spleen This is usually the case with adult negroes

Our statistics and graphs therefore of necessity bear indiscriminately on all malaria cases which have come under our observation

The etiology of a new malaria infection and that of a fever relapse in a chronic infection are evidently fundamentally different The first is directly related to the biology of the anopheles vector the latter is a consequence of the unstable equilibrium between the invading tendency of the parasite and the power of resistance of its human host

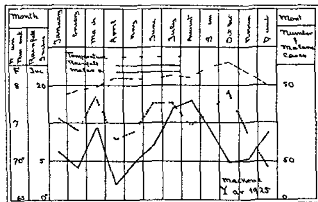
Any influence that can lower the resistance of a chronic malaria subject is liable to bring on a relapse Amongst such influences chills and trauma (contusion hæmorrhage shock surgical operation child birth etc) are the commonest The relapse of a latent infection occurs within a few hours or at the most within a few days from the chill trauma or other influence which has determined it

Amongst the population of the Guiana rivers there exist numerous conditions apt to keep organic resistance below normal level Intestinal helminthic infections are prevalent In 1923 I found 65 per cent of our employees infected with hookworm in 1925 Haslam found 66 8 per cent on the Pomeroon Poor dietary poor housing bad hygiene venereal diseases all contribute to lower the physique and resistance of the people During the rains exposure and chills are unavoidable in the carrying out of the daily native routine Malaria relapses are a frequent and immediate consequence

During January February March and April the malaria curve is perfectly parallel to the rainfall curve If the season is dry malaria cases are scarce if it is rainy they are frequent

Under average conditions the relapses tend to become more rare as immunity or better tolerance to the infection gets established This and the higher atmospheric temperature in May and June explain the persistent fall in the malaria curve (relapses mainly) during the summer rains The constant rise one notes in the malaria curve towards the end of or after the rains is evidently not in immediate relation to the rainfall We have seen the breeding habits

of *A. argyritarsis* with the summer rains and higher temperature the breeding commences and the insects become intensely active throughout the hot weather until the December rains set in. After a variable interval from the onset of the summer rains corresponding to (*a*) the time required for the development of the new generation of anopheles (*b*) the time required for the development of the *Plasmodium* in the newly infected anopheles (both (*a*) and (*b*) are directly influenced by the height of the atmospheric temperature



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and the degree of humidity) (*c*) the period of incubation of malaria in the newly infected individuals the new infection re-infections and super infections make their appearance *and the malaria curve begins to rise while the rainfall declines*

In conclusion the malaria curve as shown in our graphs is influenced by the rainfall and atmospheric temperature throughout the year but this influence varies in its mechanism of action during the first five months of the year we are

dealing mainly with relapses of malaria infections contracted during the preceding summer exposure is their main and immediate cause Immunity or tolerance to the infection is gradually established and during the latter seven months of the year relapses become rare while the seasonal increase in the insect vectors of the disease is responsible for numerous new infections and the upward trend of the curve Fig 10 which refers to the year 1925 (post epidemic) gives a vivid illustration of this different seasonal relation between the malaria and rainfall curves

In the year 1924 a slight epidemic of malaria occurred in 1926 a very serious epidemic broke out during the summer and autumn months Owing to the large number of chronic infections consequent to these outbreaks the malaria curves for the following years 1925 and 1927 respectively were very characteristically modified In the graphs for both these years one notes the most evident synchronous parallelism between rainfall and malaria persisting up to July 1925 and to October in 1927 It is only towards the end of the year (September in 1925 October in 1927) that the two curves tend to diverge from the respective rainfall curves under the influence of a relatively small number of new infections occurring as usual after the summer rains In other words the curves for the post epidemic years 1925 and 1927 are atypical owing to a vast preponderance of chronic infections in the district by far the greater number of the cases seen were relapses

The varied relation between the rainfall and malaria curves which now appear parallel and now divergent is so explained

A small number of new infections occur or at least become apparent also during the winter months these may either be new infections anopheles and chronic cases being both present in nearly every native house or they may be the result of latent infections re kindled by accidental debilitating influences

Yearly Variations in the Intensity of the Seasonal Malaria Outbreaks

The height of the malaria curve during the first half of the year when relapses of chronic infections prevail has already been dealt with the number of cases depends primarily on the severity of the malaria outbreak during the summer of the preceding year and secondarily on the general meteorological conditions rainfall and temperature (exposure to rain chills etc)

The *regime* of the malaria curve during the summer as shown in our graphs (Fig 4) is much more varied and of more difficult explanation

We have already noted the general breeding habits of *A argyritarsis* in seven years experience I have observed a great variation in the number of this species We have seen that the year 1923 was characterised by high January rains a short early summer rainy season a low aggregate *rainfall during the May October period and a very low mean* temperature throughout the year The summer malaria outbreak was very slight Anopheles were so scarce that specimens could only be procured with difficulty

In 1924 we have noted a drought during the winter (favourable condition for the survival of adult anopheles) a prolonged summer rainy season with a high aggregate rainfall during the May October period The mean temperature was low anopheles were fairly abundant during the summer but breeding was apparently slow The malaria curve showed a very marked rise two months after the onset of the rains

In 19[illegible] we similarly noted a severe winter drought a prolonged summer rainy season with a high aggregate rainfall over the May October period The mean temperature was considerably above the average while the average minimum temperature kept 3 to 4 above that of the preceding years Very soon after the onset of the rains anopheles became enormously numerous and within one month the

As we have already noted the only meteorological data available refer to rainfall and temperature - we have no information concerning atmospheric humidity in the interior It appears likely that the seasonal breeding habits of the anopheles and the strictly seasonal character of the malaria epidemics should be determined not only by temperature variation but also by the changes in atmospheric humidity The variation of these two factors in fact is more or less parallel Research in this direction is required

EPIDEMIOLOGICAL NOTES ON MALARIA ON THE FLOOD AND TORRENTIAL RIVERS OF BRITISH GUIANA

In the short preliminary notes on the physical configuration of British Guiana I made a rough division of the country into four zones running a course more or less parallel to the coast line

Passing from the sand hill to the mountainous zone the first rapids are found on the Essequebo they are situated at only forty miles from the sea on the Demerara at 100 on the Berbice at over 140 from the coast

As one passes the falls the rivers acquire quite different characters the flood is substituted for the tidal *regime* and the variations in level from bi-quotidian become seasonal the river beds are varied and broken by frequent out cropping granitic masses sand and gravel appear in the place of clay and mud the soil is less impermeable, the waters less brown and a striking change occurs in the flora and fauna

It is hardly surprising that the epidemiological *regime* of malaria should also be subject to variation amongst so modified surroundings

The study of malaria in these regions becomes particularly difficult as the population is very scarce sparsely distributed and therefore controlled with extreme difficulty

Above the rapids only very few and small permanent settlements are to be found The fluctuating exclusively male population is formed by gold and diamond diggers (pork knockers) balata bleeders and woodcutters dissemi nated over hundreds of square miles of forest The negro race prevails

The time may not be distant when the Colony will have to look to the interior for the exploitation of her as yet unsurveyed riches—timber gold diamonds other minerals balata cattle etc On the other hand even now though the number of people working or residing in this part of the interior may appear too small to warrant much attention there is no doubt that a considerable proportion of the young adult male negro population from the coast and from some of the West Indian islands at one time or another is tempted by the lure of a rapid fortune to be gained in the gold and diamond fields of the Potaro and Upper Mazaruni Of these few return with riches too many with serious and often complicated malaria

For these reasons it appears worth while to publish the following notes collected during six years experience on the Essequebo and Potaro even if they be far from complete based as they are on limited material and scanty records

The mid Essequebo river with its great length and huge bed constitutes a problem by itself At the present day it is practically uninhabited in the past important gold and timber exploitations have been carried out on its banks It is at present the main communication way with the inhabited Rupununi district and the only means of access to the Potaro gold and diamond fields

As on the tidal rivers here also we find that the banks are formed by a high dam bordering the river behind which extensive permanent forest covered swamps run to the foot of the hills and low mountain ranges which enclose the valley on either side Every year from June to August the Essequebo overflows its banks and a mighty flood

sweeps the valley from side to side The floods are the outcome of the heavy summer rains (June July) on the savannahs of the far interior where the river finds its origin

The summer rains on the mid course of the river (May June July) coincide with the great flood *They have little importance in relation to the breeding of A argyritarsis* as the rain falls on flooded country and not on impermeable clay flats to form swamps pools and puddles as it does on the low banks bordering the tidal rivers (Figs 1 and 3)

As the flood waters subside (August September) myriads of small bush covered pools are left behind and in these the breeding starts at a somewhat later date than is the case on the tidal rivers In the larger depressions along the foot of the hills large swamps persist throughout the year they are teeming with fish and have little importance as breeding sites As the small puddles dry up the active breeding season comes to an end

Fig 3 (p 6) shows the average annual rainfall curve (nine years) registered at Dadanawa on the Rupununi savannah 340 miles from the sea and the gauge measurements and the rainfall registered at Rockstone (seventy five miles from the coast and thirty five miles above the first rapids) in the year 1926 It should be noted that what is given as land level in the chart corresponds to the level of the permanent way of the terminus of the Demerara Essequebo railway which alone remains above the waters during the floods When the gauge marks 3 feet below land level the country is flooded for miles around to the foot of the sand hills which border the valley

The coincidence of flood and summer rains is already shown in Fig 3 Fig 1 (p 3) gives a schematic section of the Essequebo Valley showing the permanent surface waters and their relation to the floods and summer rains

In conclusion the surface water conditions on the Essequebo are quite different from what we have described on the Demerara and other tidal rivers The result is a

later intenser and shorter anopheles breeding season *following with remarkable regularity the periodical pulse of the great floods* Droughts on the savannahs mean a reduced flood and a healthy year

On the Potaro and without doubt on the other rivers with the same general characters such as the Mazaruni and Cuyuni we again find somewhat different conditions At present these rivers appear of greater interest as they are



Fig. 11.—Gold pit in the Potaro district holding rain water productive source of anopheles in immediate vicinity of the gold miners' camp

the centres of the gold and diamond industries thus attracting a considerable amount of labourers

The valleys are narrower bordered by steep forest clad mountain ranges The *régime* of the waters tends to be torrential with rapid changes in level and great seasonal floods The occurrence of the latter is much more irregular than those of the great Essequebo The banks of the rivers are high and the soil sandy or gravel

The general surface water conditions appear infinitely better than on either the tidal rivers or the mid Essequebo Swamps are seldom found and natural breeding sites of any importance are rare except in the immediate vicinity of *rivers and creeks*

In 1921 Bodkin found anopheles breeding in empty tins covered with vegetation and containing rain water



Fig 12 —Pit for storage of rainwater for washing auriferous gravel in the Potaro district

and in a clear grass grown stream in the locality known as Ten Miles on the Potaro road

In 1925 Haslam pointed out the danger of the diamond and gold pits as breeding sites for anopheles He collected *numerous* larvae from the muddy waters of pits where washing was actually being carried out (Figs 11 and 12) I have since been able to confirm his observations but I have failed to find anopheles breeding in tins or other water containers

The Potaro district like the Mazaruni or any other where gold and diamonds are being sought is riddled with pits of all sizes and descriptions particularly along the low lying beds of rivers and creeks Of these some are being worked the majority are abandoned lost bush covered all hold water and constitute ideal breeding haunts for anopheles

A argyritarsis is the only species I have collected in houses on the Essequebo and Potaro At Rockstone situated in the periodically flooded low land of the Essequebo Valley anopheles are plentiful all the year round with a marked increase during the hot weather following the fall of the flood This village has a well merited evil reputation

Though it is undoubted that much sickness prevails in the gold and diamond areas of the interior malaria cannot be regarded as the only or even the main responsible cause The pork knocker s life is hard and precarious—exposure poor and deteriorated food not rarely starvation poor housing bad hygiene venereal diseases alcoholism form part of his existence He breeds malaria in his camp and when sick has little to expect from the generosity sympathy or sense of *camaraderie* of his fellow workers The callousness with which the sick are regarded among these men is astonishing Diarrhœa and dysentery are very common scurvy like syndromes have been recorded Under such conditions serious and often fatal disease ensues

Potaro fever as it was called has been identified with malignant malaria My experience with cases from the Potaro does not point to a higher incidence of subtertian infection than on the Demerara The virulence of these cases is due to the conditions prevailing in the diamond fields rather than to a specifically malignant infection This is borne out by the fact that villages like Tumatumari situated on high ground on the portage over the first of the Potaro Falls and the village known as Ten Miles Potaro

both of which harbour a small permanent population are very much more healthy than either Rockstone on the Essequebo or any other locality on the tidal portion of the Demerara river

Since June 1924 I have had under observation a large timber grant situated at Butukari on the mid Essequebo twenty miles above Rockstone An average of 140 men were employed on the grant at the time of my first inspection the camp had an evil reputation as a hot bed of malaria and dysentery It was situated at about two miles from the river s edge on sandy rising ground beyond the swamp area There was then not a single latrine in the place the bush in the immediate vicinity of the camp was filthy and flies swarmed everywhere Fever diarrhœa and dysentery were rife causing a very high disability

Ten camp latrines were built at once Diarrhœa and dysentery practically disappeared *ipso facto* while the incidence of malaria fell in a very striking fashion as shown by the table below

Butukari Camp Diarrhœa Dysentery Malaria
1924 *to* 1926
(Average Labour Force 140)

Year	Disease	Jan	Feb	Mar	April	May	June	July	Aug	Sep	Oct	Nov	Dec
1924	Malaria	8	6	18	2	20	30	50	25	19	13	12	8
	Dysentery	6	9	10	10	7	5	1	0	0	1	1	1
	Diarrhœa	0	6	3	7	2	1	2	2	2	0	0	0
1925	Malaria	18	10	7	6	5	4	3	5	9	4	2	0
	Dysentery	0	0	0	0	3	0	0	0	0	0	0	2
	Diarrhœa	1	0	0	0	5	1	1	0	2	0	0	0
1926	Malaria	2	1	0	0	1	4	7	4	6	5	5	4
	Dysentery	0	0	0	0	0	0	0	0	0	0	0	0
	Diarrhœa	0	0	1	1	1	1	0	0	0	0	0	0

Beyond the general cleaning of the camp the building of

latrines and the treating of the sick no more elaborate sanitary measures were adopted

Our Butukari experiment shows what elementary hygiene can do in the prevention of malaria and for the immediate material improvement of the working capacity of the labour force to the mutual advantage of both labourer and employer

If the figures given in our table are compared with the malarial curve for the corresponding years on the Demerara river as shown in Fig 4 clear evidence is obtained proving the difference in the epidemiological *régimes* of the flood and tidal rivers While on the Demerara as a consequence of a winter drought and a heavy summer rainfall associated with a high mean temperature a serious epidemic of malaria was raging on the Essequebo in consequence of the same drought the flood was below average the river did not overflow its banks and Butukari like Rockstone and the Potaro enjoyed one of the healthiest years on record

Malaria on the Savannahs of the Far Interior

I have no first hand experience on this important subject According to reliable information collected from many quarters it would appear that locally acquired malaria is practically unknown on the savannahs

Among the Macoussi and Wapisiana Indians who have travelled to the coast as boat hands on the Essequebo or driving cattle by the Rupununi cattle trail or have bled balata in the forest areas of the upper Essequebo fever is very prevalent but tends to disappear soon after their return to the open country

Following the heavy May June rains and the excessive flooding of the savannahs mosquitoes (kinds unknown) become very numerous They feed mainly on the cattle and horses clearing of the high coarse grass for 150 feet around the ranches is said to be sufficient to protect the inhabitants from the bites of these pests

Some General Clinical Notes on Malaria in the Interior of British Guiana

Under this heading I propose to deal in a very brief way only with a few of the clinical characters of malaria which have a *more or less direct bearing on the study of its* epidemiology and with the etiology of some of its more important complications to be discussed later

Character of the fever curve —From the analysis of 1 079 fever charts referring to cases of malaria treated in Mackenzie Hospital during the period 1924 to 1928 the following figures were obtained —

Quotidian intermittent fevers	891
Tertian intermittent fevers	167
Quartan intermittent fevers	12
Afebrile malaria cases	9

The prevalence of quotidian fevers points to multiple and chronic infections clinical quartan is quite uncommon

Of 1 079 cases only 57 showed pernicious symptoms The great majority of these belonged to the convulsive type they *occurred prevalently in young children and* were frequently associated with the benign tertian parasite

The clinical findings therefore tend to confirm the prevalence of benign tertian as shown by the examination of blood films As has been stated the rarity of quartan in hospital is misleading it is the mildest of the malaria fevers and treatment is not sought until late complications have arisen When search is made by means of a house to house survey quartan is found to be quite frequent

In the clinical study of malaria on the tidal rivers of Guiana the most striking and distressing feature is the frightful persistence of the chronic infections This is particularly in evidence among the Bovianders who as we have seen with the aboriginal Indians can now be considered as the autochthonous population of the river districts

That such should be the case is hardly surprising when one considers that every house harbours hundreds of anopheles while most of its inmates are reservoirs of the infection. During the summer and autumn months re-infection or better super-infection must be an occurrence of every night.

It may well be said that the disease runs its course without any serious attempt at treatment ever being made. The hopelessly small doses of quinine distributed at long interval by the more or less incompetent and unconvinced dispensers to whom the care of these districts is entirely entrusted are little more than a drop in the ocean. They only serve to instil and fortify the conviction now widely spread among the natives that quinine or at least the Government quinine tablet is useless.

Since the epidemic of 1936 hundreds of children and adults along the rivers of Guiana have scarcely passed a week without fever. Many of such cases are still ill and under observation at the time of writing (1939). In the presence of such misery the term chronic infection appears scarcely adequate to express so extreme a degree of malarial saturation.

Conclusions

(1) Malaria is hyper-endemic in the river areas of the interior of British Guiana.

(2) All three types of malarial parasites are found. In a series of 1,247 positive blood films 81.4 per cent showed *P. vivax*, 15.7 per cent *P. falciparum* and 2.9 per cent *P. malariae*.

(3) The incidence of *P. malariae* is in reality very much greater. In laboratory routine large rings are currently diagnosed as *P. vivax*. While relatively rare in hospital *P. malariae* is found commonly in house to house survey.

(4) The reported vector of malaria on the coast is *A. tarsimaculata* whose breeding sites are situated in grassy

swamps clogged drains and trenches in open country in both sweet and brackish waters

(5) The vector of malaria in the interior is *A argyritarsis* which breeds in forest covered swamps and puddles and tends to congregate in houses

(6) *A tarsimaculata* has been found on rare occasions in the interior but only in areas in which the bush had been cleared and never in houses According to Bonne and Bonne Wepster this species is not a malaria carrier in the interior of Surinam

(7) The epidemiology of malaria in the interior of British Guiana is mainly governed by the breeding habits of *A argyritarsis* in adaptation to the topographical and meteoro logical conditions Localities situated at only a small distance may present perfectly different conditions and characters as regards malaria

(8) On the tidal rivers like the Demerara Berbice lower Essequebo Pomeroon Morucca etc the breeding sites are situated on the mud flats bordering the rivers The height and distribution of the local rainfall and the height of the mean temperature regulate the time intensity and duration of the breeding season and indirectly the malaria epidemic curve

Droughts during the winter months have a direct influence on the epidemiology of malaria by favouring the mass survival of adult female anopheles from one breeding season to the next

The December January rains have no influence on the breeding of anopheles apparently in relation to the lowered mean temperature On the contrary they are the direct cause of destruction of numerous adult insects and are indirectly responsible for a large number of malaria relapses from exposure in chronically infected individuals

(9) On the great flood rivers like the Essequebo *A argyritarsis* is also the vector Its breeding sites are found in the myriads of small puddles and temporary swamps left

by subsiding floods these are the outcome of the rainfall on the savannahs of the far interior and are characterised by clock like regularity *The fall of the flood begins some* time after the peak of the summer rains on the mid course of the rivers so that the anopheles and malaria seasons on the Essequebo are somewhat delayed in respect to those of the tidal rivers but much more regular in their time of occurrence intensity and yearly succession High flood and high temperature would appear as the most dangerous condition on the mid Essequebo Local rains have little or no importance Droughts in the interior by affecting the floods bring healthy years

(10) On the smaller flood rivers with a more torrential character as the Potaro and Mazaruni the natural configura *tion of the valleys appears much less favourable to mos* quitoes and malaria *A argyritarsis* is the vector gold and diamond pits scattered all over the immediate vicinity of the camps are the most dangerous breeding sites

Bad hygiene bad food exposure venereal and other diseases dog the existence of the gold and diamond digger and contribute to give to these naturally favoured localities an evil reputation

(11) *With an exact knowledge of local conditions and by a careful systematic study of meteorological data throughout the colony it is possible to forecast by some weeks or even months the greater or less gravity of the seasonal malaria outbreak*

(1) Clinically quotidian intermittent fevers are the commonest form observed 8 9 per cent in 1 074 fever chart

(13) Pernicious syndromes are relatively rare more common in children in whom convulsions are frequent and often associated with very heavy *P vivax* infections

(14) Extreme chronicity intensified by continual re infec tion and super infection leading to a veritable malarial saturation constitutes the main clinical characteristic of the disease on the tidal rivers of Guiana

PART II

BLACKWATER FEVER IN THE INTERIOR OF BRITISH GUIANA

In Part I I have described in some detail the general characters of the inhabited inland districts of British Guiana in relation to the epidemiology of malaria. Malaria is hyperendemic in these regions with a very marked prevalence of the benign tertian type over the other malarial parasites. In spite of the great uniformity of the climate throughout the year malaria shows a marked seasonal periodicity in relation to the breeding habits of *A. argyritarsis* the main carrier in the interior. This species in fact though common all the year round only breeds during the hottest months of the year—from June to November.

During seven years observation covering nearly 10 000 cases of malaria mainly from the mid Demerara and Essequebo and from the Potaro rivers a considerable variation has been noted in the importance of the annual malarial outbreaks. Such variations I have ascribed to the corresponding irregularities in the amount and distribution of the rainfall and to the height of the atmospheric temperature both of which have a direct bearing on the intensity and duration of breeding of the carrier of the region.

In spite of this high endemicity of malaria according to the official medical statistics blackwater fever would appear as a rare disease in the colony. The figures on p. 49 are extracted from the Annual Reports of the Surgeon General and Registrar General during the years 1922 to 1927.

These figures are misleading. In my experience on the Demerara river blackwater is a common disease. The

Year	Total Incidence of Malaria	Cases of Blackwater treated in Public Hospital	Deaths from Blackwater Registered
[illegible]	[illegible]	[illegible]	4
[illegible] 3	1 080	11	6
[illegible] 4	1 148	3	[illegible]
[illegible] 5	1 054	4	7
[illegible]	1 234	11	8
[illegible]	[illegible]		[illegible]

serious epidemic of malaria which swept through this district during the latter part of 19[illegible] afforded a particularly favourable opportunity for the study of this and other malarial complications and sequelæ. Blackwater in Demerara shows both clinically and epidemiologically some particular features which may render the following notes not only of local but also of general interest

Incidence of Blackwater in Relation to Malaria

During the year 19[illegible]3 which presented typical average meteorological characteristics malaria was very mild on the Demerara river no case of blackwater was recorded (see Fig 4)

The early months of 19[illegible]4 were very dry the rains broke in May and persisted throughout the summer reaching their maximum in July. The mean temperature remained low averaging 81 F during the summer months. A fair outbreak of malaria occurred and [illegible]40 cases were treated during the August December period

During the winter 19[illegible]4 to 19[illegible]5 following this little epidemic chronic relapsing benign tertian infections were common throughout the district. Blackwater now made its appearance and four cases were recorded (one in October two in November 19[illegible]4 and one in January 19[illegible]5) with two fatalities

In 1925 meteorological conditions were of average character and malaria was correspondingly mild No further cases of blackwater were recorded Fig 4 records graphically the malaria and blackwater *incidence for the period 1926 to* 1928

Under the influence of a prolonged drought during the first eight months of 1926 the incidence of malaria was exceptionally low and during the January September period no cases of blackwater were registered The unusual meteorological conditions for this year and their influence on the serious malaria epidemic which swept through the district during its latter months have already been described

In October the incidence of malaria rose suddenly and remained exceptionally high to the end of the year Between October and December no less than 1 160 were treated in our hospital and dispensaries During this period *only four cases of blackwater were recorded with two fatalities*

In 1927 chronic relapsing infections were extremely prevalent The malaria curve fell progressively from a maximum of 290 cases in January to a minimum of 100 in December in all 1 952 cases were treated the great majority of which were chronic benign tertian infections Forty cases of blackwater were admitted to our wards of these five proved fatal

During 1928 malaria was mild 1 538 cases were treated Chronic infections dating back to 1926 were still common five cases of blackwater were recorded with no fatality

The chart (Fig 4) shows clearly the relation of blackwater to malaria absent when malaria is low present but rare when malaria is prevalent common as a late consequence of malaria epidemics One notes moreover that the blackwater fever curve is not parallel to the one of malaria In 1926 the malaria curve touched its maximum in November when only one case of blackwater was registered The vertex of a hæmoglobinuria curve occurred in August 1927 In other words hæmoglobinuria was rare during the acute

phase of the malaria epidemic while it became more and more common during the following ten months as the influence of persistent chronic infections made itself felt. The greatest number of cases were seen in August 19[illegible]7 when with the occurrence of the new seasonal malaria outbreak re-infections took place in individuals already suffering from chronic infection. Under the same influence one *again notes the appearance of a few cases of blackwater* during the August-October period in 19[illegible]8. In 192[illegible] with an average malaria curve but with chronic malaria still common in the district two cases of blackwater occurred in January with no fatality.

Types of Malaria Parasites found in Cases of Blackwater in British Guiana

In the interior of British Guiana the prevalent form of malaria throughout the year is the benign tertian. During the 19[illegible]6 to 19[illegible] period the result of routine blood examinations performed in Mackenzie hospital gave *P. vivax* 81.4 per cent, *P. falciparum* 15.7 per cent, *P. malariae* [illegible]9 per cent; double infections were found in 4.3 per cent of cases.

P. falciparum occurs particularly in the autumn months. It is found more commonly when the meteorological conditions during the summer are such as to prolong the active anopheles and malaria season into the late summer and autumn. We thus find that in the latter six months of 19[illegible]6 when such conditions were realised *P. falciparum* accounted for [illegible] per cent of positive blood films. In 19[illegible]7 and 19[illegible]8 instead it only accounted for 13 per cent and 10.[illegible] per cent respectively.

In a series of fifty-six cases of blackwater fever the following are the results of blood examination for malaria parasites (thin film method):

Examinations	5[illegible]
Positive for malaria parasites	19

Positive for *P vivax*	15
Positive for *P falciparum*	4
Negative	37
Percentage of *P vivax* in positive films	79 per cent
Percentage of *P falciparum* in positive films	21

From the above figures it appears that 33 9 per cent of the cases gave a positive blood examination 26 8 per cent were infected with *P vivax* 7 1 per cent with *P falciparum* Among nineteen blackwater cases giving a positive blood examination the ratio between *P vivax* and *P falciparum* infections (79 per cent against 21 per cent) differed only slightly from the one found in the examination of blood films from plain malaria cases collected during the same period

It should be noted that during the last six months of 1926 when *P falciparum* was unusually common only four cases of blackwater were registered In 1927 when *P falciparum* had fallen to 13 per cent of malaria infections and when intense chronic benign tertian malaria was rife blackwater rose to its maximum with forty cases

Residence in the Endemic Area

Our fifty six cases can be classified as follows as regards the country of origin of the patients —

Interior of British Guiana (Demerara river)	46
Coast lands of British Guiana	[illegible]
British West Indian Islands	2
Surinam	1
Europe	[illegible]

Eighty two per cent of our patients belonged to the native

population of the Demerara river district where malaria is hyper endemic

Incidence of Blackwater in the Various Races

For a better evaluation of the figures to be given under this heading it is necessary to consider first the relative numbers of the various races in the district. Deeks and James working exclusively among labourers of the Canal Commission were able to produce exact figures for the purpose of comparison with their blackwater statistics in Panama. On the Demerara river hæmoglobinuria is essentially a disease of the uncontrollable riverine population: any attempt to estimate the relative numbers of the various races settled along the river would be mere guess work. I believe that a very fair idea of the ethnographical constitution of the population of the district can be obtained from the analysis of admissions to Mackenzie hospital for medical diseases.

On a total of 3 617 patients we find the following racial *distribution*

Negroes	1 854 or 51 2 per cent	
Mixed races (Boviandérs)	1 037	28 6
Aboriginal Indians	367	10 3
White races (other than Portuguese)	127	3 5
Portuguese	*10*	*0 3*
Chinese	17	0 4

Of the Negroes approximately 40 per cent were natives of the British West Indian Islands particularly Grenada and St Lucia. In these islands though malaria exists it is much less common and serious than in Demerara. Most of the islanders I have examined soon after their arrival in the Colony presented a negative history for fever: they invariably got infected after a few months

The following figures refer to our fifty six cases of blackwater classified according to race and sex

Race	Males	Females	Total
Negroes	7	2	9
Mixed races	19	13	32
Aboriginals	4	1	5
East Indians	3	3	6
Europeans	3	0	3
Portuguese	0	0	0
Chinese	1	0	1
	37	19	56

A comparison of these figures with the number of patients treated for each race respectively should give a fairly accurate idea of the incidence of blackwater in the various races in the Demerara river district

Race	Number [illegible]	Number of Blackwater cases	Ratio of Blackwater per cent
Negro	1,854	9	0.4
Mixed races (Bovianders)	1,037	3	3.0
Aboriginals	357	5	1.4
East Indians	209	6	[illegible]3

For European and Chinese the numbers are too small for consideration

We find in conclusion that blackwater in the interior of British Guiana is essentially a disease of the native population of the hyper endemic malarial area (Bovianders and aboriginal Indians) that it is rare in the negro race also among the numerous recent immigrants from the West

Indian islands who possess no acquired immunity or tolerance to malaria infections

It is here interesting to note that Deeks and James found blackwater very rare among the Panamanians of mixed blood in spite of their being heavily infected with malaria

Age Distribution

Our series of blackwater fever cases can be classified as follows as regards the age of the patients —

Children below 15 years	33
below 1 year	1
2 to 10 years	3
11 to 15	9
Adults	23
16 to 30 years	12
31 to 60	8
over 60	8

The disease is most prevalent among young children This fact is all the more striking considering that children in these inland districts are scarce as the greater part of the population is formed by temporarily immigrated adult males It is interesting to note the different incidence of blackwater in the two sexes at different ages in thirty three cases occurring among children below fifteen years we find 58 per cent males and 4 per cent females Out of twenty three cases occurring in adults 72 per cent were males and 28 per cent females This can be explained partly by the preponderance of the male element in the population (not so marked among the Bovianders) and partly by the much less arduous and exposed mode of life of the women The youngest patient seen was a six months old infant of mixed race The oldest a seventy seven year old white Creole [1] who had lived for over fifty years in the

[1] Creole in British Guiana [illegible] white [illegible] born in the Colony The [illegible] of white Creole East Indian Creole Chinese Creole [illegible] The term [illegible]

district enjoying good health He contracted malaria during the 1926 epidemic and dragged on a chronic constantly relapsing infection refusing quinine for the much loved purgative treatment of the Creoles He died within thirty six hours from the onset of hæmoglobinuria

Blackwater Fever Families

Among the riverine population of Demerara the tendency of blackwater to occur among the members of the same *families is striking*

E R Whitmore has reported on a similar tendency in Cuba Five families accounted for no less than 23 2 per cent of the cases I saw in the whole Demerara river district

Family No 1 —Cornelius of mixed Indian Negro and white blood consisting of the parents and four children Three of the children suffered repeatedly from hæmoglobinuria at different periods

Family No 2 —Duclos of Indian Negro and White blood parents and three children All the children suffered repeatedly from blackwater at different times

Family No 3 —Edmonds of Indian White and Negro blood mother and three children All the children suffered from blackwater and one died of the disease

Family No 4 —Giddings East Indian parents and three children Two children had blackwater with several relapses

Family No 5 —Perreira mixed Portuguese and Negro blood parents and four children The father and one child suffered from blackwater

The members of a family all living together are exposed to the same infection (house disease) On the other hand *the possible existence of a family* idiosyncrasy in the mechanism of production of hæmoglobinuria in chronic malaria is suggestive G Thompson considers that blackwater is not due to a direct action of the malaria parasite or any other organism but is to be regarded as a reaction of the body to prolonged infection It is probable that family idiosyncrasy

should play a part in the mechanism of such a reaction but further material is required before any well based conclusion can be drawn tropical America with its very peculiar ethnographical characteristics appears as the most fertile field for research

Clinical Characteristics of Blackwater Fever in British Guiana

I have used the term blackwater fever exclusively in reference to cases presenting hæmoglobinuria Cases showing dark brown urine from bile pigments with a negative spectroscopic examination for hæmoglobin have not been included How nearly such a condition is related to blackwater may be shown by the following case

J J a Negro age twenty five native of Grenada came to British Guiana in June 19 3 Had not suffered from malaria in his native island contracted it in 1923 in the diamond fields of the upper Mazaruni river suffered from repeated attacks with bilious vomiting and slight jaundice In January 19 4 he was employed by our company and worked steadily for one year with only five days disability for fever Two weeks before being admitted to hospital the patient stated he had suffered from slight fever much headache and pain on the left side on the day preceding admission he passed some dark brown urine He travelled to hospital covering ten miles on an ore train and doing the last mile on foot Admitted January 13th 1925 General condition good muscular development powerful slight jaundice *liver normal the spleen reaches the transverse umbilical* line it is soft and exquisitely tender (unusual symptom in a Negro) Tongue coated bowels open regular nothing otherwise noteworthy Temperature normal pulse 76 respirations 18 Blood examination reveals a heavy infection with *P vivax* Urine clear at the time of admission a sample brought by the patient passed the preceding evening is of a dark brown colour and contains 6 per 1 000

albumin There is no characteristic sediment froth on shaking greenish spectroscopic examination negative for Hb

The case appearing as a simple one of bilious malaria quinine was administered in ten grain doses twice daily

Subsequent Course —The temperature remained normal throughout and the general condition fair The urine became dark brown and heavily albuminous with a regular forty eight hour periodicity coinciding with an exacerbation of the splenic symptoms In the intervals the urine was clear and showed no albumin On the sixth day after the third paroxysm of biluria the dose of quinine was increased to 30 grains in the twenty four hours The following day at noon the patient passed some typical dark red urine presenting all the characters and reactions of blackwater The paroxysm persisted for twelve hours quinine was suspended The following day the urine was clear but within forty eight hours from the onset of hæmoglobinuria a new paroxysm occurred but the urine had again acquired its bilious character the paroxysms continued with regular tertian periodicity after the seventh attack the periodicity became quotidian for three days Quinine was again administered on the eleventh day (gr 30 *pro die*) The malaria parasites which had persisted throughout in the blood now disappeared the urine became normal after the fourteenth day and the patient was discharged five days later

In our blackwater cases jaundice was very common In the majority it was slight with a pale diffuse lemon colour of the scleræ in others it was more intense In two fatal cases in European patients infected with *P falciparum* the jaundice was so intense as to remind one of that observed in complete obstruction of the bile duct

The great majority of the cases of blackwater I have seen in British Guiana are mild and often very mild I have known of many cases who never sought medical treatment and who recovered sometimes after two or three relapses

In a small percentage of cases on the contrary the disease may be extremely violent and death ensue within a few days or hours In the following instance the disease ran a fulminant course —

A nineteen year old Barbadian Negro was taken suddenly ill in one of the labour camps and died within a few hours from the onset of the disease before it was possible to convey him to hospital Post mortem examination revealed numerous small sub epicardial echymotic effusion spleen twice its normal size kidneys slightly enlarged *œdematous their surface of section was of a uniform deep wine red* colour the limit between the two substances and the corticle pattern being obliterated The bladder was found full of typical dark red urine Microscopic examination of the urinary sediment and of stained sections of the kidney confirmed the diagnosis of blackwater

All cases in which blood examination revealed a sub tertian infection appeared as much more severe In our series of 50 cases nine deaths were registered (1[illegible] per cent) of these three occurred from six to twenty four hours after admission In cases showing a *P vivax* infection the death ratio was 3 15 in cases showing *P falciparum* it was [illegible] 4

In one at least of the three fatal cases giving a negative blood examination there was strong suspicion of a malignant infection as both the wife and son of the patient examined at the same time showed heavy *P falciparum* infection the former with numerous crescents In conclusion —

Total deaths in 50 cases of blackwater	9
Deaths in 10 cases showing malaria parasites	6
Deaths in 15 cases showing *P vivax* infection	3
Deaths in 5 cases showing *P falciparum* infection	3
Deaths in 37 cases showing a negative blood	3

According to race the fatal cases can be classified as follows Negroes 3 mixed races (Bovianders) aboriginal Indians 1 Europeans Chinese 1

It is interesting to note that the Negroes among whom the disease is rarest show the highest mortality (three deaths in nine cases of blackwater in a total of 1 804 Negroes admitted to hospital as in or out patients) The Bovianders on the contrary who are the most susceptible to the disease present *a much lower mortality (two deaths* in thirty two cases of blackwater in a total of 1 037 cases admitted)

As regards age we find that of nine fatal cases four occurred in adults and five in children below fifteen years of age The mortality among the adults was 17 3 per cent against 15 1 per cent in children

The disease invariably occurred in individuals particularly children with a history of persistent relapsing practically untreated malaria of many months duration The blackwater attack would supervene during an ordinary attack of fever Most of the patients travelled many miles by canoe and finally walked into hospital in spite of their condition

The factors which precipitated the blackwater attacks were varied exposure and chills were the commonest In the case of an elderly European of very strong constitution residing in the colony for twenty years with a history of very mild malaria hæmoglobinuria was brought on by exertion and exposure to the sun In the case of an Italian labourer who had resided in the Guianas for six years and who was literally *soaked* with malaria the attack was brought on by acute alcoholism He had been dismissed from hospital after a sharp attack of subtertian malaria with sufficient quinine for two weeks treatment *He* was reported to have thrown away the drug and to have drunk a tumblerful of proof alcohol with kitchen salt in it as a more efficient cure He was brought into hospital the same night with the most violent attack I have witnessed and died the *next* day

In another European case (not comprised in this series)

the patient was seen by me for a severe attack of benign tertian malaria. Some weeks later he died of blackwater in another hospital in consequence of acute alcoholism. Other similar cases have occurred within my knowledge.

Alcoholism must be regarded as a very important factor in the etiology of blackwater amongst Europeans in British Guiana.

Amongst the cases observed the disease showed a very marked tendency to relapse at intervals, the attacks becoming gradually milder. At the end of 1927, fifteen months after the malaria epidemic, blackwater had again become a rare disease, and most of my old patients, after months of nearly continuous fever and occasional attacks of hæmoglobinuria, were beginning to pick up immunity, or better tolerance having become established. I never observed a fatal case during a recurrence of the disease.

In each individual attack one or more paroxysms of hæmoglobinuria might occur. Sometimes a single paroxysm would last for two or three days, the urine passing through the classical colour stages; in others paroxysms would present a quotidian or a regular tertian periodicity. Relapses while in hospital were frequent. In one case four were noted over a period of fifty four days. The influence of quinine in carrying on such relapses was repeatedly noted.

Treatment

I have now adopted the practice of withholding quinine in all cases of blackwater, whether malaria parasites be present in the blood or not.

In view of the frequent association of blackwater with the *benign tertian parasite* I have adopted *stovarsol* for the standard treatment of the disease. The drug is well tolerated by both children and adults; it has a decided action on *P. vivax* without danger of precipitating further attacks of hæmoglobinuria.

With the exception of cases admitted *in extremis*, the drug

has given very good results The small number of cases in which the disease was undoubtedly associated with *P falciparum* is insufficient to allow one to form any idea on the efficiency of stovarsol in similar cases We have seen that the disease was always particularly violent in the presence of malignant infection

The general treatment was symptomatic aiming at supplying as much liquid as possible water plain or alkaline and barley water *per os* and saline *per rectum*

Four or five days after all signs of hæmoglobinuria had disappeared the cautious administration of quinine was begun starting with doses of 1 grain or less and slowly and progressively working up to full doses before the patient was discharged The patient was advised to continue the treatment for some months but to suspend it immediately in the case of recurrence of blackwater fever

Conclusions

(1) During seven years observation (1922 to 1929) in the interior of British Guiana on the mid Demerara and Essequebo rivers and in the Potaro district fifty six cases of blackwater fever were observed

(2) The disease was absent during the years in which malaria was mild it appeared as a rather rare condition in years of average malarial severity it became very common after an epidemic which prevailed amongst the population of the tidal rivers during the latter months of 1926

(3) The epidemic curve of blackwater during the period of observation did not coincide with the curve of malaria The apex of the former occurred ten months after that of the latter

(4) In the interior of British Guiana benign tertian malaria accounts for 81 per cent of all malarial infections

(5) *P vivax* was found in the blood of 26 8 per cent of blackwater cases *P falciparum* in 7 1 per cent negative results were returned in 66 1 per cent

(6) Negroes present a remarkable immunity to the disease This does not appear in the form of acquired immunity as it is just as apparent among Negroes born and bred in the hyper endemic malarial river districts as in newly immigrated Negroes from the coastal towns and the mildly malarial West Indian Islands Out of fifty six cases nine only occurred in Negroes Among 1 854 Negro patients the incidence of blackwater was 0 4 per cent

(7) Blackwater in the interior of British Guiana is most prevalent amongst the permanent riverine populations constituted mainly by people of mixed blood (Boviunders) and aboriginal Indians all of whom are born and bred in the hyper endemic malarial area Out of fifty six cases thirty seven occurred in patients of mixed race or in Aboriginal Indians In a total of 1 03? patients of mixed race the incidence of blackwater was 3 per cent

(8) Blackwater in Demerara appears prevalently as a disease of children Out of fifty six cases thirty three were observed in children below fifteen years of age

(9) The tendency of blackwater to recur in the same families has been noted Five families accounted for ?3 ? per cent of all the cases registered

(10) Though severe and even fulminant cases have been recorded the majority are mild Cases showing *P falciparum* were invariably much more severe

(11) Relapses are frequent and usually tend to become progressively milder as tolerance to the chronic infection is gradually acquired

(12) The general mortality among fifty six cases was 16 per cent The death ratio for cases showing a *P falciparum* infection was 2 4 against 3 1 for *P vivax* The mortality was highest among Negroes who as a race were by far the least susceptible to the disease On the contrary mortality was lowest for the Boviunders or mixed races amongst whom the disease was most prevalent

(13) No fatality was registered in relapsed cases

(14) Stovarsol has been used with very satisfactory results in the treatment of hæmoglobinuria. It has a decided action on the benign tertian parasite without involving the risk of precipitating a new attack of blackwater.

Experience with this drug in cases of hæmoglobinuria associated with *P. falciparum* has been too limited for coming to any definite conclusion as to its value under such conditions.

Some General Observations on Blackwater

Without going into the literature in detail and considering *only the more recent and now classical works on the subject* one finds some interesting differences in the experiences of the various authors who have studied hæmoglobinuria under different malarial conditions.

In Panama, where malignant tertian accounts for approximately 80 per cent. of all malaria infections, Deeks and James found blackwater common, particularly among the Southern *European labourers employed by the Canal Commission*. These authors, from a very complete study of the problem, conclude that the incidence of hæmoglobinuric fever is in direct proportion to the intensity of estivo-autumnal malaria. The possibility of benign tertian malaria causing blackwater is not denied but doubted. As regards cases of hæmoglobinuria presenting *P. vivax* in the blood the importance of preceding subtertian attacks and the possibility of a double infection are emphasised.

J. Gordon Thompson, in his recent research in Southern Rhodesia, found *P. falciparum* responsible for 94.6 per cent. of all malaria infections. *As regards blackwater he concludes* that it is due to repeated attacks of *P. falciparum* alone.

He regards *P. vivax* findings in the blood of blackwater patients as cases of double tertian subtertian infection in which *P. vivax* tends to persist throughout the hæmoglobinuric attack, in consequence of the lesser degree of

damage it produces in the red blood corpuscles which thus escape destruction

Most authors who have worked on this disease on the west coast of Africa (where malignant tertian accounts for an average of at least 90 per cent of all infections) have connected the disease with *P falciparum* a view which is now adopted by the more recent issues of the leading text books

In 1913 Lovelace in Brazil at Porto Velho in the Matto Grosso found in 16 431 cases of malaria 9 155 positive bloods (55 7 per cent) Of these *P falciparum* accounted for 65 4 per cent *P vivax* for 30 1 per cent double tertian subtertian infection for 4 3 per cent and quartan for 0 2 per cent

In similar conditions he registered 383 cases of black water of which 178 or 46 5 per cent gave a positive blood examination *P falciparum* occurred in 48 9 per cent *P vivax* in 41 6 per cent double infections in 9 0 per cent The author insists on the *extreme tenacity* and the diabolical resistance of the tertian infections

R R Nutter who worked with Lovelace describes black water at Porto Velho as much milder than that seen in Panama with a lower mortality Many of the patients entered hospital with a history of several previous attacks from which they had recovered without medical attention These patients were mostly Spaniards working on grading contracts remote from hospital

Cerebral types of malaria were relatively infrequent among the labourers These conditions described by Lovelace and Nutter in Brazil are remarkably similar to what I have described for the interior of British Guiana with the notable difference that in British Guiana the incidence of benign tertian malaria is very considerably higher (81 4 per cent)

I believe that the respective *rôles* of *P falciparum* and *P vivax* in blackwater can be summarised as follows keeping

in mind the particular malarial conditions of the different countries in which hæmoglobinuria has been studied —

(1) In countries showing a high preponderance of *P falciparum* over *P vivax* infection (West Africa—Panama) hæmoglobinuria is essentially a complication arising from repeated attacks of subtertian The benign tertian parasite when found in the *great majority of cases can be regarded* in the light of a double infection

(2) In countries showing a high incidence (Porto Velho) or a heavy preponderance (interior of British Guiana) of benign tertian infections characterised by great chronicity and continuous tendency to relapse blackwater is frequent but usually in a mild form

(3) In Demerara a higher mortality has been noted among blackwater fever cases associated with *P falciparum* (2 4) than in cases associated with *P vivax* (3 15)

(4) The ratio of *P vivax* to *P falciparum* infections found *in the blood of blackwater patients is practically the same as* what is found among malaria patients in the same locality and during the same period (Porto Velho British Guiana)

(5) In Demerara hæmoglobinuric fever follows at a distance of several months the malaria epidemic becoming apparent among the most obstinate cases of benign tertian and commonly among young children belonging to the population of the endemic area It does not coincide with the season of high incidence of *P falciparum* infections Subtertian infections have little tendency to relapses

(6) Double infection which can be easily admitted as a mere contingence *with malaria conditions similar to those* of the west coast of Africa can scarcely be invoked in conditions such as those described by Lovelace and myself We should otherwise be driven to conclude that the greater the incidence of double infections the milder blackwater fever becomes This is evidently paradoxical!

Double infection being simply presumed in many instances cannot be disproved definitely

It is indisputable that *P falciparum* is the parasite most commonly responsible for hæmoglobinuria and conversely that hæmoglobinuria is endemic where *P falciparum* prevails but an intense prolonged benign tertian infection can in the long run lead to the same results What *P falciparum* can produce by acute mass action *P vivax* can cause by a slower more continuous process The action of the two parasites can be compared to the acute and cumulative poisonings which some substances such as arsenic are known to produce

The damage caused by *P vivax* to the red blood corpuscles is much less serious than that caused by the malignant parasite The destruction of parasitised cells is therefore less rapid and less massive This would explain on the one hand the greater mildness of the clinical symptoms and on the other the frequent persistence of the parasite in the peripheral blood throughout the attack

PART III

MALARIAL ALBUMINURIA AND NEPHRITIS IN BRITISH GUIANA

Endemic Nephritis of British Guiana

THE annexed table has been compiled from data obtained from the annual reports of the Surgeon General and Registrar General of the Colony —

Year	Number of cases of nephritis treated in public hospitals			Deaths from nephritis		Death rate per mille	
	In-patients	Out-patients	Total	Hospitals.	Colony	Of all Deaths.	Of estimated population.
1918	874	—	—	[illegible]	1 238	98 1	3 9
1919	791	—	—	193	971	78 [illegible]	3 1
1920	601	—	—	172	835	105 9	2 7
1921	681	—	—	196	892	96 9	[illegible] 6
1922	745	—	—	24[illegible]	958	110 5	3 1
1923	776	—	—	184	841	99 3	2 7
1924	726	—	—	221	753	97 5	2 5
1925	976	1 713	2 689	214	815	110 8	2 6
1926	763	1 411	2 174	190	669	84 2	2 1
1927	760	834	1 594	195	661	82 3	2 1
Total	7 693	3 958	11 651	2 099	8 633	96 3	2 7

These figures can only be taken as a rough index of the incidence of nephritis in British Guiana. Most of the deaths which occur in the interior of the Colony are not certified by medical men; the cause of death is assigned by the

dispenser acting as registrar for the district often simply on the information supplied by the relatives of the deceased

Among the natives simple backache is regarded as a sign of kidney disease and the word Bright s along with biliousness bad feelings and worms is one of the commonest heard from patients of all descriptions during routine consultation

In some cases registration is done by outlying police stations and the entry concerning the *causa mortis* is left to the imagination of a native sergeant Such data enter into the general statistics after having been more or less revised

Also deaths which have been certified by medical practitioners must be considered with a certain amount of reserve confusion between albuminuria and nephritis is common many cases showing œdema not of renal origin are diagnosed as Bright s disease

The above statistics regard essentially advanced cases requiring hospital treatment They fail to give an adequate idea of the very much larger numbers of patients in whom the kidney disturbances are transitory slight or not yet of sufficient importance to invalid the patient which are treated in plantation hospitals by private practitioners by the ubiquitous dispensers or by the quacks who infest the Colony

Though the excessively high incidence of nephritis in British Guiana has been noted since many years the actual amount of study which has been given to it is scarce and strictly limited to statistical clinical and anatomical observations carried out in patients or at autopsies in the hospital of Georgetown

Daniel in a series of 9?6 autopsies of malaria cases found renal disease in ?.8 In a recent statistic given by Stevens Grace found on twenty four cases of nephritis the following conditions acute nephritis in one instance chronic paren

chymatous nephritis in seven chronic interstitial nephritis in sixteen cases

The diseased native of British Guiana will do his best to keep out of hospital as long as he possibly can It is only when totally disabled that he will seek admission

The great majority of cases of nephritis seen in the coastal hospitals and in Georgetown in particular are chronic cases of long standing in which the disease has reached an advanced if not an extreme stage of evolution From the above statistics in fact we see that approximately 12 per cent of admissions die in hospital Crace s post mortem findings point to the same conclusion In such cases it is presumable that the primary cause which determined the nephritic process was in action months or even years before the patient was admitted All traces of such a condition may have been lost in the interval

At the same time from what is known of nephritis secondary *to specified diseases or conditions the clinical and anatomical* findings once the disease is established and advanced are more or less identical whatever the original cause may have been Given a case of advanced chronic nephritis in any part of the world be it a patient in a hospital ward or a body on the autopsy table one could hardly presume to advance anything more definite than a guarded hypothesis as to the primary cause which induced the disease How much more difficult must the investigation be of any particular such condition if it is carried out in the hospitals of a large and crowded town where cases and diseases congregate from all parts where life and habits are more complicated *more strained where the isolation of a* clinical case in its history and environment is practically impossible

Chronic nephritis is the outcome of a large number of more or less known toxic and toxi infective conditions Such conditions evidently *would tend to prevail in a large* town and in a series of patients admitted to hospital cases

of different etiology would be bound to occur though in variable proportion

I believe that these are the main reasons for which the cause of endemic nephritis in British Guiana has so long eluded discovery The solution of the mystery would have without doubt been simple had its study been undertaken in the limited ecological field of a rural district or sugar plantation where the problem would have been strictly circumscribed and the evaluation of every single element infinitely more simple

Soon after my arrival in British Guiana at Mackenzie on the Demerara river I was struck by the frequence of high degree albuminuria in a considerable proportion of the labourers applying for employment by our company At the same time cases of chronic nephritis were common both in the in and out patient department of our hospital

It occurred to me that conditions at Mackenzie were exceptionally favourable for a systematic study of albuminuria and nephritis and their relation to other diseases and conditions

Three villages harbouring about 1 500 inhabitants under strict sanitary and medical control and a district of approximately 8 000 inhabitants equally dependent on us for medical assistance constituted the field of action Systematic records were kept of all physical examinations of labourers and of in patients and out patients seen in hospital for all diseases

In seven years work a large mass of material has been accumulated and for most of our patients a fairly well documented history can be obtained often covering several years this is particularly the case with children and with the West Indian islanders who come to us directly from their homes remaining at our works for some years *General conditions of life have been also investigated* We now have sufficient data for the adequate study of every case in itself and in its environment

The present research has been divided as follows —

(1) Albuminuria in West Indian adult male labourers in British Guiana

(2) Albuminuria in relation to heavy manual labour in West Indian Negro labourers in British Guiana

(3) Albuminuria in malaria fevers in British Guiana

(4) Malarial nephritis in British Guiana

(5) A short revue of the literature on malarial albuminuria and nephritis

(6) Malarial nephritis and its clinical forms

Albuminuria among West Indian Labourers in British Guiana

During the period 1920 to 1928 I have had the opportunity of examining a large number of West Indian male adults mainly of Negro race for the selection of labourers for the Demerara Bauxite Company

In order to attribute a proper value to the following figures it is necessary to note that a certain selection had already been made by the employment officer before the men were sent up for examination Our figures therefore cannot be taken as relating to the average adult West Indian male population At the same time the standard of the mass of the applicants for employment was far below that of military fitness

The routine examination included an analysis of the urine for albumin by the cold nitric test During the last three years all cases giving a positive result were again tested with sulfo salicylic reagent

During eight years 9 510 men were examined Of these nine tenths were Negroes the ages ranged from eighteen to forty years with a few exceptions below and above these extremes The great majority were between twenty and thirty years old

A large proportion of these labourers were not natives of British Guiana For comparative purposes it is of interest

to classify the men according to their country of origin Unfortunately careful records on this point have only been kept since 1907 but considering that our labour force has approximately presented an uniform constitution throughout the whole of the period mentioned an analysis of the last 1 000 cases should give a fairly reliable index for reference

In the last 1 000 consecutive examinations we find the following distribution —

British Guiana	513	or	51 3 per cent
British West Indian Islands	450	or	45 0
British India	37	or	3 7

The 450 West Indian Islanders can be further classified as follows —

Saint Lucia	173	or	17 3 per cent (of the total)
Granada	113	or	11 3
Barbados	46	or	4 6
Saint Vincent	31	or	3 1
Trinidad	26	or	2 6
Tobago	24	or	2 4
Dominica	19	or	1 9
Other	18	or	1 8

In 9 510 examinations 428 cases showing albuminuria were registered *i e* a general rate of 4 5 per cent The quantity of albumin was very variable 0 5 per 1 000 being the most frequent finding

Cases showing very large amounts 6 to 12 per mille were surprisingly common With rare exceptions the albuminuria was not accompanied by other abnormal clinical signs Frequently it was found in individuals presenting splendid physique and powerful muscular development

In 144 cases in which a record of the locality of origin was kept we find the following distribution —

British Guiana	77	or	53 5 per cent
British West Indian Island	67	or	46 5

Of 77 cases from British Guiana 54 5 per cent belonged to the country districts and 45 5 per cent to the city of Georgetown The 67 cases registered among islanders present *the following* distribution and relative percentages in respect to the total of 144 cases —

Saint Lucia	20	or	14 6 per cent
Grenada	9	or	6 2
Barbados	14	or	9 2
Saint Vincent	9	or	6 2
Trinidad	7	or	4 9
Tobago	2	or	1 3
Dominica	-	or	1 3
Other	4	or	2 8

With the exception of Barbados we find that *the rate of* albuminuria is approximately proportionate to the number of natives examined for each country In other words its distribution is fairly uniform and apparently independent of the country of origin

The figures for Barbados *are unfortunately too* small for much weight to be given to their apparent discrepancy from the others It may be noted that Barbados is the least malarial of all the West Indian Islands and that most of the Barbadians examined had resided for a long time in British *Guiana The islanders who showed protein in their urine* with few exceptions had resided in the colony for over one year

In order to carry out some more exact observations in 1926 fifty unselected consecutive cases showing albuminuria *at examination were kept (under observation) in* hospital for two days under the following routine —

(1) History Clinical examination Blood pressure Examination of blood films for malaria and filaria Stool examination for helminthes Hecht reactions for syphilis

(2) *Collection of urine for* twenty four hours—amount

reaction gravity urea albumin qualitative and quantitative test sediment

(3) Urea concentration test by McLean's technique Water elimination (Martinet) test

As regards age and race these cases could be classified as follows —

Age	Number	Race	Number
1 to 20 years	9	Negro	40
21 30	33	Mixed race	7
31 40	"	East Indian	3
41 45	1		—
	—		50
	50		

History — The majority of cases gave a negative history as regards disease or symptoms which might be ascribed to renal disorder Nearly all admitted having suffered from malaria six had large spleens Yaws was frequent in the remote history of many of the islanders but not among the Demerarians Gonorrhœa was admitted by the majority six gave a history of suppurated inguinal adenitis or abscesses Enlarged epitrochlear and groin glands were nearly always present

Out of fifty only five i e 10 per cent gave a history pointing to renal disease All these five had suffered from persisting intermittent fever with ague chills bilious vomiting lumbar pains and profuse sweating after some time œdema of the face and ankles appeared In one instance the patient had gone to hospital with general anasarca Of these five cases four contracted the disease in the diamond fields on the upper reaches of the Mazaruni river

All the men (fifty) with the exception of two declared themselves in good health at the time of examination and to have been healthy and strong having always been engaged in heavy manual labour The fine physique and muscular development of the majority testified to the truth of these statements

Clinical examination —The teeth were bad in the majority as is the rule among the natives The apex beat was situated outside the nipple line in three cases Blood pressure (by Pachon s oscillometric and the auscultatory method) was within normal bounds in thirty two instances The maxima showed a tendency towards the upper limit *(140) in eleven cases*

It was decidedly high (150 to 200 mm) in sixteen cases and abnormally low in two *(110 mm) Such figures must* however be interpreted with reserve as high readings are very common among the normal powerfully developed Negro labourers

The examination of blood films for malaria parasites was constantly negative For *Microfilaria bancrofti* 13 4 per cent positive findings were returned

Stool examination showed 41 5 per cent infected with hookworm 15 per cent with ascaris 14 per cent with trichuris and 7 2 per cent with strongiloides

These findings concerning helminthic infections are below average for Demerara natives as shown by comparison with the figures obtained from routine examination of all patients admitted to Mackenzie Hospital and from surveys conducted on the Demerara river or in other districts of the colony

The Hecht reaction for syphilis in a series of 39 cases gave the following results *negative 24 positive 10 not* readable 5 Out of 34 cases in which the reaction was read able 10 or 29 4 per cent were positive Such a figure is considerably above the average rate deduced from routine examination of all patients admitted to hospital On 730 Hecht reactions the following results were registered negative 75 7 per cent positive 10 2 per cent not readable 14 1 per cent *Better results have been obtained* by the Meinicke flocculation reaction—on 900 consecutive *tests 19 7 per cent positive returns were registered*

The large number of non readable reactions which con stitute a serious handicap in the use of the Hecht reaction

in British Guiana is due to the very low titre of complement in a high percentage of the unheated sera resulting in lack of hæmolysis in the control tube. This complement deficiency is particularly remarkable in the East Indian race.

Not much weight can be given to this abnormally high rate of positive Hecht reactions among our albuminuria subjects as the number is small and the high percentage of ambiguous readings invalidate the results.

Urine examination.—Cases showing pus in the urine evidently of urethral or bladder origin have naturally not been included in this investigation.

The urine was usually clear, frequently showing a few heavy filaments, reaction acid, specific gravity from 1 010 to 1 0 0, in two instances it reached 1 030. The amount passed in twenty four hours varied; it was below 1 000 c c in twenty five cases with a minimum of 450. It was above 2 000 c c in four cases. Polyuria was marked in two cases with 3 750 and 4 650 c c respectively. Of the last two cases while both history and physical examination of the one gave negative results, in the other the patient stated that he had suffered from persistent malaria in the upper Mazaruni river, the last attack having ended only ten days previously to my examination.

In the fifty cases examined the amount of albumin varied from a trace to 2 per mille. As has already been stated much higher readings (6 to 10 per mille) were not rarely observed in routine examinations also among apparently fit applicants for employment. In three cases the albuminuria presented a typical orthostatic character, disappearing with rest and coming on with exertion.

The urea concentration test by McLean's method, carried out in uniform conditions of diet, rest, etc., gave variable results. On forty four cases tested twenty five or 56·8 per cent gave a normal concentration. In the rest readings were below 2 per cent; of these ten cases gave a concentration above 1 5 per cent, in three instances it was below 1 per

cent Of the latter one gave a negative history the patient presenting a fine physique with only a slight outward displacement of the *ictus cordis* The other two both gave histories of prolonged fever contracted in the upper Mazaruni river accompanied by œdema of the face and ankles

Two cases which gave an evident history of kidney disease appearing after prolonged intermittent fevers gave a normal concentration test

No information was gained from Martinet s water elimination test The mode of elimination was most irregular not only in albuminuric but also in normal control subjects

In conclusion the cases of albuminuria we have studied fall into three main groups —

(1) Transitory albuminuria in relation to position (orthostatic) or exertion

(2) Permanent albuminuria of slight entity with negative history and negative clinical and laboratory findings

(3) Permanent albuminuria (*a*) with a history of a recent attack of malaria fever (highly coloured urine with increased specific gravity and lowered amount, or sometimes polyuria) (*b*) with a remote history of dropsical symptoms arising in the course of a persistent untreated malaria infection The albuminuria may be very heavy frequently unaccompanied by other urinary changes The concentrating power of the kidney is frequently unimpaired and the general health and physique excellent

Albuminuria among Negro West Indian Labourers engaged in Heavy Manual Work

For an investigation on the influence of exertion in determining albuminuria among *West Indian labourers* a gang of seventy men engaged in hand loading of ore at Akyma Mine was selected This gang presented the advantage of being employed in hard but standardised work The men in fact were employed by task, and each one loaded with

very fair approximation 8 tons a day Only Negroes of selected physique were used on this job

For testing the urine salicyl sulphonic acid was used

Every one of the men had presented a negative test for albumin at the time of engagement

The experiment was carried out by testing for each man (*a*) the urine passed at 6 a.m. before the starting of the day's work (*b*) the urine passed at the end of the day's task implying ten hours work for the shifting of approximately 8 tons of ore

The results of the experiment can be summarised as follows —

(*a*) Number examined	70
(*b*) Number presenting albumin at time of employment (after many days rest)	Nil
(*c*) Number presenting albumin before commencing the day's work (having been engaged on same hard work for many days previously)	11
	or 15.7 per cent
(*d*) Number showing albumin at end of day's work	17
	or 24.2 per cent

These figures are very striking as a demonstration of the importance of exertion as a provocative cause of albuminuria We find in fact that out of seventy men selected only for their physical fitness and strength and presenting normal urine when examined after prolonged rest 24.2 per cent become albuminuric at the end of a hard day's work and in 15.7 per cent under the influence of the continued work albuminuria becomes permanent being still present on the following morning

Further investigations for the purpose of determining what influences may contribute to favour this albuminuria from effort are yet to be carried out

MacLean in the examination of 60 000 men belonging to the British Army found 5 per cent with albuminuria In 2 per cent the amount of protein was marked in 3 per cent it was slight

In 9 510 West Indian *natives mainly of Negro race* examined in Demerara at rest I have found albuminuria in 4 5 per cent

The incidence of albuminuria among West Indian native labourers would appear if anything below average

In 200 men examined after strenuous exercise MacLean found that the incidence of albuminuria increased from 7 to 14 per cent Among seventy West Indian labourers of strong physique and presenting normal urine when examined at complete rest I have found albuminuria in 24 2 per cent after a day of hard work and in 15 7 per cent a night s rest was not sufficient to restore the urinary function to normal albuminuria becoming permanent as long as they were engaged in heavy work

These findings are not sufficient to allow of drawing definite conclusions It appears at any rate that the West Indian Negroes do not present an abnormal tendency to albuminuria when examined at rest Whether exertion is *more prone to cause albuminuria in these natives than in* the average European soldier remains to be confirmed as further comparable data are required on both sides

Albuminuria in Malarial Patients

The following observations were carried out on unselected in and out patients seen in Mackenzie Hospital during the period 1926 to 1929 Only cases giving a positive blood examination for malaria parasites have been considered The urine was examined by the cold nitric test and in *positive cases again* by the salicyl sulphonic reagent

For hospital patients a twelve hour (night) specimen was collected For out patients the urine was passed at the same time as the blood film was made

General incidence.—In 550 cases of malaria with positive blood findings 138 showed protein in the urine. The general incidence was therefore 25 per cent.

Relation to duration of infection.—Albuminuria is rare in new or recent infections. It is impossible to supply reliable figures separating new from relapsing chronic infections when working among natives. But considering the general incidence of albuminuria among malaria cases seen month by month during the 1926 epidemic we find that albuminuria was rare during the first three months when the epidemic was in its acute stage and new and recent infections prevailed. It gradually increased and became very prevalent as the epidemic curve began to decline and the chronic infections assumed the upper hand.

In the following table the figures relating to the number of malaria cases treated give an idea of the general trend of the malarial epidemic curve. Note the progressive increase in the incidence of albuminuria which reaches its maximum five months after the epidemic has reached its height.

Year	Month	Number of Malaria Cases Registered	Incidence of Albuminuria among Malaria Cases
	May	25	—
1926	June	50	—
	July	110	—
	August	150	13 5 per cent
	September	140	13 6
	October	380	10
	November	400	30
	December	380	23 8
1927	January	290	39
	February	230	24
	March	190	47
	April	140	38
	May	190	33

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Two years later when the influence of the 1926 epidemic was nearly but not completely exhausted we find that the incidence of albuminuria has fallen tending towards the pre epidemic figure For the first four months of 1929 we thus find albuminuria in 18 1 per cent of malaria cases

Natives of the West Indian Islands who arrive in our district with a negative history for malaria and present a normal urine at the time of employment usually contract malaria soon after their arrival

During the first attacks the urine remains normal it is only after they have come up repeatedly with fever that protein appears in the urine

Relation of Albuminuria to the various malarial parasites — The 550 cases we have examined can be classified as follows according to the species of plasmodium found in the blood —

P vivax	Ring stage only	388
	Heavy infections with all stages present	59
P falciparum		67
P malariæ		24
Double infection—*P falciparum* and *P vivax*		12

Our 138 cases showing positive blood for malaria parasites and albuminuria can be classified as follows —

P vivax	Ring stage only	83
	Heavy infections with all stages present	29
P falciparum		14
P malariæ		11
Double infection—*P falciparum* and *P vivax*		1

From the preceding figures we find that the incidence of albuminuria in the various malaria infections is very different

As regards *P vivax* one finds a very marked difference according to the severity and duration of the infection In 388 examinations showing light infections with the

[illegible]	[illegible]	Number of cases [illegible]	[illegible] cases [illegible]
P vivax	41[illegible]	11[illegible]	[illegible] per cent
P falciparum	6[illegible]	14	[illegible]
P malariae	[illegible]	11	4[illegible]
Double Infection	1	1	8

parasites prevalently in the ring stage eighty three showed albuminuria *i e* 21 4 per cent

In fifty nine cases instead showing heavy infections with all stages of the parasite in the circulating blood no less than twenty nine or 49 per cent showed albuminuria

We find in conclusion that albuminuria is more frequently associated with the benign form of malaria In quartan the incidence of albuminuria is approximately twice as great as for the two other species In chronic intense benign tertian malaria the incidence of the condition is very much higher than in recent or light infections or than in subtertian cases

(These figures may require a certain amount of revision as during the early part of the investigation a considerable number of light quartan infections with the parasite in the ring stage may have been classified as *P vivax*)

Albuminuria in Malaria in relation to race —The total of 550 cases examined can be classified as follows in regard to the race of the patients —

Negroes	340	Ratio per cent to total examined (550) 61 8 per cent
Mixed races	133	24 [illegible]
Aboriginal Indians	31	[illegible] 7
East Indians	[illegible]	5 3
Europeans	1[illegible]	2 [illegible]
Portuguese	3	0 [illegible]
Chinese	2	0 3

The racial distribution of the 138 cases showing a positive blood with albuminuria was the following —

Negroes	75	or	54 4 per cent
Mixed	40	or	29 0
Aboriginals	12	or	8 7
East Indians	10	or	7 2
Europeans	—		—
Portuguese	—		—
Chinese	1		—

The relative incidence of albuminuria in each race is shown in the following table —

R[illegible]	N[illegible] Examined	Numb[illegible]	N[illegible]mbe[illegible] with Alb[illegible] [illegible] Examined
Negroes	340	75	22 per cent
Mixed	133	40	30
Aboriginals	31	12	29
East Indians	29	10	34 4

From the preceding figures it appears that albuminuria is found in all races but with a different frequence

The Negro appears considerably less prone to it than the others the East Indians present the highest liability but the number examined is relatively small Of all the Guiana races they are without doubt those who have the *most evident signs of chronic malaria Most of them belong to the rural districts of the coast or to the sugar* plantations

Relation to sex and age—The 550 cases on which this examination bears can be classified as follows as regards age and sex —

Ages	Males	Females	Total
Below 15 years	48	35	83
16 to 45 years	372	73	445
Above 45 years	22	—	22
	442	108	550

Classifying correspondingly our 138 cases presenting albuminuria we find —

Ages	Males	Females	Total
Below 15 years	17	19	36
16 to 45 years	74	15	89
Above 45 years	13	—	13
	104	34	138

As regards sex the incidence of albuminuria would appear somewhat higher (31 per cent) among females than among males (23 per cent) But if one considers that the greater part of the female cases occurred in children the importance of sex as a predisposing cause appears dubious

The incidence of albuminuria in the various age groups on the contrary is interesting —

Below fifteen years on 83 cases examined 36 showed albuminuria Incidence 43 3 per cent

Sixteen to forty five years on 445 cases examined 89 showed albuminuria Incidence 20 per cent

Above forty five years on 22 cases examined 13 showed albuminuria Incidence 60 per cent

Relation to treatment.—Albuminuria is rare also in chronic cases of long standing which take more or less regular quinine treatment This is probably the reason

why it is not commonly seen among Europeans in spite of the widely spread malaria infection in this race

Clinical—In the series of cases we have considered the amount of albuminuria was variable. It has not been attempted to separate the cases showing more or less definite signs of renal involvement from those presenting no further urinary symptoms beyond the temporary passage of



FIG 13—Malarial œdema not of renal origin in two year old Aboriginal Indian child

protein. The passage between these two conditions is scarcely defined. Under the present heading I propose to deal only with those cases in which signs of serious renal damage were not in evidence (Fig 13)

The amount of albumin is usually slight from a faint trace not measurable by the current quantitative tests to ½ or 1 per 1 000

The urine is more or less highly coloured and scarce In early cases albumin appears intermittently with the fever disappearing with the apyrexial interval Patients who have been in hospital repeatedly first for fever then for fever with intermittent febrile albuminuria and who continue to neglect themselves soon come back with fever and permanent albuminuria When the condition reaches this stage other signs become apparent and the term plain albuminuria is scarcely appropriate

In a large proportion of cases which take treatment or which show a greater resistance to the infection which only gives few and slight relapses albuminuria usually disappears with the fever and frequently does not reappear even if fever relapses

The question of general constitution concomitant infections (helminthiasis syphilis) dietary chronic intoxications housing conditions general hygiene etc all must be considered as secondary factors which by influencing the persistence and relapsing of a chronic malaria infection may indirectly have a bearing on the development and subsequent course of renal disturbances

The marked difference we have noted in the incidence of albuminuria among the various races can find its explanation in the habits and tendencies of the various people more than in an actual difference in racial susceptibility

Conclusions—(1) The general incidence of albuminuria in a series of 550 unselected cases of fever showing malaria parasites in the blood was 25 per cent

( ) Albuminuria is rare in patients suffering from a recent infection it is a frequent manifestation of chronic relapsing untreated malaria

(3) In relation to a malaria epidemic the incidence of albuminuria tends to increase during the months following the acute stage of the outbreak as the incidence of chronic relapsing cases tends to prevail on new infections

(4) Albuminuria is most frequent in quartan infections

(46 per cent) and in chronic benign tertian infections (25 per cent) It is less common in subtertian (20 per cent)

(5) It is relatively less common among Negroes (22 per cent) than among other races Mixed 30 per cent Aboriginal Indians 29 per cent East Indians 34 4 per cent

(6) It is more frequent among children (43 per cent) and among elderly patients (60 per cent) than in young adults (sixteen to forty five years 20 per cent)

(7) It is rare in cases submitting to quinine treatment also if irregular

Malarial Nephritis in the Interior of British Guiana

During seven years observation from 1923 to 1929 inclusive 102 cases of nephritis were admitted to the wards or were seen in the out patient department of Mackenzie Hospital

For comparative purposes the exposition of the study of these cases has been disposed on the same plan already followed in the description of blackwater in this district during the same period By the repeated reference which will be made to this disease I do not mean to suggest that blackwater has any direct relation to chronic nephritis in British Guiana but simply to demonstrate that the con ditions which lead to the appearance of blackwater and chronic nephritis are one and the same

Incidence of Nephritis and its relation to Malaria and Blackwater Fever—We have seen that malaria was extremely mild on the Demerara river during the year *1923* *No cases* of blackwater or of nephritis were observed (see Fig 4)

In 1924 a fair malaria epidemic occurred during the summer many infections *contracted during this outbreak* continued to relapse throughout the following year and the epidemic curve for 1925 was characterised by an unusual *height during the winter months* with *more or less marked* falls and rises in direct and immediate relation to the seasonal climatic conditions (Relapses from exposure see Fig 10

p 31) Blackwater made its first appearance with one case in October two in November and one in January 1925 In 1924 one sporadic case of nephritis was registered in January and one more in September In 1925 seven cases were seen with the following distribution one in January one in March one in October three in November and one in December

The first six months of 1926 were characterised by a very low incidence of malaria no case of blackwater occurred up to September During the latter part of the year a veritable pandemic of malaria swept through the district Black water again made its appearance four cases being registered during the last three months During the first nine months of 1926 three sporadic cases of nephritis were observed

The epidemiology of malaria in the district during the years 1927 and 1928 was completely dominated by an enormous prevalence of ultra chronic relapsing cases The number of cases seen and re seen monthly was very high Blackwater which in the first four years of my residence in the district had been a rare disease became quite common no less than forty cases occurring in 1927 and six in 1928 Since the 1926 epidemic nephritis has occupied a prominent place in the nosology of the district up to the time of writing not a month has passed without cases being seen Five cases occurred in the last four months of 1926 while the epidemic was still at its height twenty three cases were recorded during 1927 fifty two in 1928 twelve in 1929

These facts are graphically demonstrated in our chart The relation between the three diseases malaria blackwater and nephritis is most evident blackwater and nephritis become apparent as soon as the malaria curve rises becoming all the more common during the post epidemic period when chronic infections abound (1927 1928 and 1929) Also under such conditions both the diseases tend to abate during the month of least malarial incidence while immediate

exacerbations follow the seasonal rises of the malarial curve (re infections)

Blackwater after reaching its maximum of incidence nine months after the height of the malarial epidemic tends to disappear within little more than a year The nephritis curve is much more steady and prolonged reaching its maximum approximately 2 years after the peak of the malarial epidemic At the end of 1929 at a distance of nearly three years from the malarial epidemic of 1926 but with chronic malarial infections dating back to that period still a prominent feature among our patients nephritis is still very frequent

Types of Malaria parasites found in cases of Nephritis in British Guiana—In a series of eighty seven cases of *nephritis the following are the results of blood examination* for malaria parasites (Thin film method)

Cases examined		87
Positive for malaria parasites	61	70 per cent
Negative for malaria parasites	26	30

The sixty one positive cases can be grouped as follows

P vivax only	40	65 5 per cent
P malariæ only	17	28
P falciparum only	1	—

Double infections

P vivax and *P falciparum*	2	6 5
P vivax and *P malariæ*	2	

Comparing these figures with those found in the examination of 1 247 positive malaria blood films during the 1926 to 1929 period a roughly approximate idea can be obtained of the relative incidence of nephritis in each particular form of malarial infection

P it	Number 1 47 Positi Malaria Films 19 8- 9	Number in 83 Cases M lari 1 Nephriti Posi tive Blood	Rati
P vivax	1 016	43	4 23 per cent
P falciparum	1)6	—	—
P malariæ	35	17	48 57

In the preceding statistics the following points are worthy of particular notice —

(*a*) The very high incidence of positive bloods among nephritic patients (70 per cent) as compared with the findings among plain cases of clinical malaria during the same period (40 per cent) by the simple thin film method

(*b*) The absence in nephritic bloods of *P falciparum* as a pure infection while during the same period this parasite accounted for 15 7 per cent of positive blood films from malaria cases In two instances it was found associated with *P vivax*

(*c*) The extremely high incidence of *P malariæ* in the blood of cases of chronic nephritis (28 per cent) compared with its relatively low incidence among plain malaria cases (9 3 per cent) on the other hand the enormous proportion of quartan malaria cases in which kidney disease was present (48 57 per cent)

It is here important to mention again that the incidence of *P malariæ* among malaria cases in general and in nephritis in particular is much more frequent than our figures would imply based as they are on the examination of one single blood film per patient Many ring infections must have been attributed to *P vivax* which in reality should have been diagnosed as *P malariæ* Repeated examination will in future be carried out so as to establish this important point

The influence of residence in the endemic area—Our 107 nephritic patients all belonged to the Demerara river district

but they can be classified as follows as regards their country or locality of origin —

Demerara River district	67
City of Georgetown	9
Guiana Seacoast	8
West Indian Islands	16
India	1
Syria	1

65 6 per cent of our cases were therefore natives of the hyper endemic malarial river area

Incidence of Nephritis in different races—Our 102 cases can be classified as follows according to race —

Rac	M les		F m les		Total		T tal
	Adults	Childre	Adults	Childr	Adults	Children	
Negro	32	2	2	2	34	4	38
Mixed races	11	7	6	13	17	20	37
Aboriginal In	7	2	1	2	8	4	12
East Indian	3	3	1	3	4	6	10
Portuguese	2	—	—	1	2	1	3
Chinese	—	—	—	1	—	1	1
Syrian	1	—	—	—	1	—	1
Total	56	14	10	2.	66	36	102

It is here again necessary to recall the peculiar ethno graphical characteristics of the district The Negro element is mainly constituted by temporary immigrants and children and women are relatively very scarce Our figures show that the disease is common among male adult Negroes no less than thirty four out of a total of thirty eight cases occurring in adults and thirty two in males

It is interesting to note that the West Indian islanders show no greater tendency to the disease than the native Negroes of British Guiana Of our thirty eight cases twenty two were Demerarians and sixteen recently immigrated

islanders The proportion of West Indian islanders among the labourers on our works as we have seen is 45 per cent

Among the mixed races (Bovianders) which constitute the permanent population of the river areas we find a much more uniform and natural distribution of both sexes and of children in relation to adults the disease is common in both sexes and at all ages tending to prevail in young children Similar conditions are found among Aboriginals and East Indians

In consideration of the very un uniform proportion of the different races among our hospital patients a comparison of the number of cases of nephritis registered for each race to the approximate number of cases of that particular race treated during the period should give a more accurate idea of the liability of each individual race to kidney disease

R	N mbe E ml 1f ll J 1 as s (19 9)	N mb f Cas f N ph iti	I 11 f N phritl
Negro	1 854	38	2 04 per cent
Mixed Races	1 037	37	3 56
Aboriginals	357	12	3 36
East Indians	209	10	4 83

Making allowance for the peculiar conditions prevailing for the Negro race we find that the incidence of the disease is fairly uniform only among the East Indians its occurrence seems to be somewhat greater

It is interesting to note that nephritis unlike blackwater is as common in the Negro race as in the others

Age distribution —Our cases can be classified as follows as regards the age of the patients —

Children below 15 years		37
below 1 year	—	
1 to 10 years	31	
11 to 15	6	

Adults	65
16 to 20 years	15
20 to 45	41
over 45	9

These figures also are influenced by the preponderance of adult males in the Negro population The Negroes in fact account for thirty eight cases only four of which were children Considering all cases therefore we find that only 36 per cent of our patients were children If we consider exclusively the natives of the district constituted essentially by mixed races we find that the disease tends to prevail in children who account for no less than 54 per cent of cases

The relation of sex and age is also interesting With the exception of the Negro race for the reasons I have already mentioned we find that while among males the disease occurs in adults twice as frequently as in children for the women the reverse takes place and out of twenty eight cases twenty occur in children and only eight in adults

We find in conclusion that among the river population nephritis prevails among the children but not to so marked a degree as blackwater adult females appear less liable to the disease evidently in relation to the lesser amount of exposure which their life and occupations require

Clinical notes on cases of Nephritis —No cases of typical acute nephritis have come under my observation in British Guiana The 102 cases on which these notes are based present the characteristics of sub chronic and more commonly of chronic dropsical or interstitial nephritis

(1) *History* —Without exception every case gave a history of chronic relapsing nearly continuous malaria The greater part of the patients had enjoyed good health up to the last month of 1926 when they contracted malaria during the epidemic The fever had practically never left them

since relapsing continually with the slightest exposure or exertion

Treatment had invariably been rudimental represented by *inadequate doses of quinine taken for short periods and at long intervals and by repeated purgation with laxatives of* all kinds and descriptions

Some cases are stated to have suffered only from slight but very persistent fevers which did not keep them from work and for which they did not find it necessary to seek treatment In such cases *P malariae* was invariably found *in the blood*

Blackwater figured in the history of only one case In no case were other diseases beyond malaria in evidence the possible relation of such diseases to nephritis will be examined later

The main clinical character of the malaria infection in all these cases was not its intensity during the fever attack but its long drawn persistence and inexorable tendency to *relapse This we have seen is the main clinical characteristic of malaria in British Guiana*

The sequence of nephritis in chronic relapsing malaria is most evident in the case of infants and in the recently immigrated West Indian Negroes reference should be made to the individual case reports given at the end of this book

Relation of Albuminuria and Nephritis in Malaria patients We have seen that in British Guiana albuminuria is exceptional in patients who are suffering from a newly acquired *malarial infection* it is likewise rare *in* individuals who though affected with chronic malaria take sufficient quinine to maintain the disease more or less under control *Albuminuria makes its appearance only after the malaria parasite has been actively at work in the organism for some time*

In many cases particularly among the Negroes tolerance to malaria seems to establish itself within a few months though the disease is not extinguished and can become

apparent under favourable conditions its clinical activity comes to an end and to all purposes the patient appears as cured In such cases albuminuria which may have been present during the first relapses as an intermittent phenomenon disappears with the other manifestations of the disease the kidney escapes without damage On the contrary in cases of persistent chronic relapsing malaria which tend to evolve for long periods continually fomented by re infections and by the infinite accessory and accidental agencies which form part of the routine in the life of the native *albuminuria which at first is only a sign of kidney* fatigue appearing as a transitory condition accompanying or following the febrile paroxysms soon establishes itself as a permanent condition *the amount of protein per mille* gradually increases as new relapses occur casts and white cells appear in the sediment and sooner or later the patient complains of slight œdema of the ankles and face nephritis is established

Any agency tending to stop the progress of the malarial infection during these early stages will cause a speedy resolution of the kidney symptoms and a permanent cure may ensue But if the disease is allowed to evolve unhindered and untreated generalised œdema and anasarca with all the complex symptomatology of chronic parenchymatous or chronic interstitial nephritis gradually establish themselves The lesions of the kidney become permanent and irreparable and all chances of recovery are forfeited

I have repeatedly followed this sequence in the evolution of malaria and kidney lesions in patients whom I have been able to *observe over a period of several years*

It is not easy to establish the time of onset of the actual kidney disease the process is so gradual and subtle as to *be hardly appreciable* If we consider that during the first months of the malarial epidemic albuminuria was relatively scarce among fever patients (10 per cent October) that nephritis began to be noted as a frequent disease six months

after the peak of the malaria epidemic that it has since continued to be common to the end of 1929 reaching its maximum of incidence in the last three months of 1928 at two years distance from the malaria epidemic that no cases of nephritis were registered in infants below eighteen months of age in spite of the fact that during the 1926 and 1927 period infants invariably contracted malaria within a few days or weeks from their birth that nephritis was common among children of two and three years of age we have a considerable amount of elements outlining the evolution of the disease as a whole from which we can surmise that albuminuria and established chronic nephritis are only different phases of the same process of slow progressive deterioration of the kidney under the continuous onslaught of a long drawn more or less evident but always active malarial infection exacerbated by frequent recurrences and sustained by repeated re infection

Symptomatology —Our cases can be classified in two main groups in relation to the prevalence of the malarial or of the nephritic syndrome

Cases in which the main complaint is relapsing intermittent fever of long duration without external evident signs of renal disease

Such cases are very liable to be overlooked by a superficial examiner or in overworked hospitals The primary malarial nature of the disease is evident and sufficient to explain the anæmic and asthenic condition of the patient Investigation is rarely carried beyond blood examination

By routine investigation of both blood and urine in all my malaria patients I have been able to detect quite a considerable number of these early cases who constitute the connecting link between the plain albuminuria of the early stages of a chronic infection and established nephritis

I have found by practice that the presence of *P malariæ* in the blood of a chronic fever patient is a strong and rarely fallacious reason for suspecting the presence of kidney

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The clinical characters of these cases are remarkably uniform The onset of the dropsical symptoms is usually described by the patient as fairly sudden always during an attack of fever or immediately after it The œdema is soft and frequently imposing involving the face the legs the genitals and abdominal wall serious effusion in the peritoneum is constant and may be of a very considerable degree In young children the eyes may be completely closed and the scrotum and prepuce so distended as to appear translucent Dyspnœa and orthopnœa are present

The urine is scanty highly coloured cloudy loaded with albumin (° to 15 per cent) its density is usually low averaging 1 010 to 1 012 The sediment is formed by a large number of granular and hyaline casts renal cells leukocytes red cells are exceptional

The U C test shows serious reductions in the concentrating power of the kidney the diastatic test gives parallel readings Headache is exceptional vomiting is rare and only in relation to a malarial attack The whole clinical picture is dominated by the dropsical symptoms and their mechanical consequence The state of nutrition and general condition of the patients particularly children is fair None of our cases could be described as cachectic

In another group the œdematous manifestations are scarce but more persistent the patients are more anæmic and complain of frequent headache occasional vomiting and dizziness Their albuminuria is of average intensity 1 to 4 per cent the sediment is scarce with hyaline and granular casts and very few cells The density of the urine is low 1 010 and the amount of urine passed 2 000 to 3 000 c c and more in twenty four hours

The patients complain of pollakiuria and nicturia Blood pressure is increased and signs of cardio vascular alterations are present

involvement All these patients complain of is persistent fever and debility with occasional transitory slight swelling of the ankles at night and of the face in the morning

The amount of urine passed is below normal usually highly coloured with a density somewhat above average and acid reaction Albumin may vary from ¼ to 2 or 3 per mille The sediment contains abundant hyaline and granular casts few renal elements and leukocytes no red cells The urea concentration test frequently shows normal concentration more often the concentrating power of the kidney is impaired The diastatic test equally shows impaired kidney permeability In adult subjects blood pressure is not increased and there are no clinical signs of cardio-vascular involvement

Under appropriate treatment with the improvement of the primary malarial disease the kidney condition rapidly mends as is evidenced by the progressive fall of the amount of protein the gradual disappearance of sediment and the parallel improvement in the readings of both the U C and diastatic tests

These patients nearly invariably return after a short period with established nephritis having ceased the treatment as soon as the fever and other symptoms abated The conception of *latent disease and preventive treatment does* not find place in the mentality of the British Guiana native

Cases of established Nephritis—In the great majority of cases which have come to our hospital with nephritis dominating the clinical picture chronic malaria was still a very prominent factor not only in the history but in the actual disease with the following classical and unmistakable symptoms intermittent quotidian tertian and quartan fever splenomegaly and abundance of malaria parasites in the peripheral blood In a small percentage of very old standing cases I have seen which came to us from other hospitals a clear relation to malaria infection could not be established with any certainty, and the patients appeared

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In such cases the onset of the disease is usually much more gradual The fever though persistent and of long standing is described as low or internal it never disabled the patient or kept him from his work He therefore never troubled to get treatment Also the first signs of kidney disease were mild the patient often states to have noted slight œdema of the ankles and to have suffered from headaches for many months back without serious impediment to his work and activity

In both the preceding groups of cases I have found malaria parasites practically constantly In the first group corresponding to the classical symptoms of chronic parenchymatous nephritis both *P vivax* and *P malariæ* are found in the second corresponding to the chronic interstitial type of slow evolution *P malariæ* appears to prevail

These patients are much less amenable to treatment than the early cases the kidney appears much more deeply and irreparably damaged the general clinical picture is that of an established chronic and interstitial nephritis In what exact relation these two groups stand to each other cannot be said with any degree of certainty it appears probable that the secondarily contracted kidney constitutes the ultimate stage of evolution of malarial nephritis How much time is required for the reaching of such a stage cannot be stated one of my cases with a chronic quartan infection of two and a half years duration and presenting the syndrome I have described in a typical form died while in *hospital from an intercurrent lobar pneumonia* post mortem examination revealed a characteristic secondarily contracted kidney

I have at present under observation two more similar cases in which the duration of the disease *is approximately* the same In one *P malariæ* in the other *P vivax* was found

The well known very slow evolution and long duration of this form of nephritis which according to post mortem

reports appears to be the commonest in British Guiana must be kept in mind in the study of the etiology of the disease Malaria even if untreated gradually tends to extinguish itself a glance at our general chart shows clearly how also the consequences of a pandemic which deeply modified the malarial curve for over two years tend to disappear by the third year and the malarial curve resumes its normal form in 19 9 Even in the most obstinate infections tolerance and even immunity gradually develop and evidence of malaria tends to disappear but the irreparable lesions of the kidney remain or even continue to evolve under secondary or accidental agencies It is certain that most of the cases I have at present under observation presenting patent evidence of both active old standing malaria and chronic interstitial nephritis will appear as simple nephritic cases if again examined or seen at autopsy in three four or ten years time

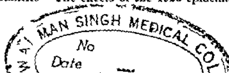
Clinical course—Once definite nephritis is established unless prompt and energetic treatment is instituted the disease tends to evolve progressively Each new attack brings on an exacerbation of symptoms which abate *in parte* and slowly after the attack subsides the condition of the patient becoming progressively worse as the recurrences repeat themselves

Termination—Death may supervene during an exacer bation of the disease due to a malarial relapse with sudden onset of renal insufficiency and cardiac failure

In advanced cases uræmia and coma end the disease In œdematous patients the uræmic symptoms usually appear at the very last stage Cases of pure azotemic nephritis with out œdema and prevalent uræmic sydrome are rare only one such case has come under my observation

Optic complications have not been observed

Intercurrent diseases of which lobar pneumonia is the most important are responsible for a large proportion of fatalities The effects of the 1926 epidemic on the Guia



rivers will probably reveal themselves during the next four or five years

Prognosis —The primary etiological factor of the disease being established as a chronic malarial infection of the tertian or quartan type powerful and specific therapeutic means are at our disposal Such findings alter fundamentally the general outlook as regards prognosis

The formulating of the prognosis rests esentially with the stage of evolution of the disease or better with the degree of damage the kidney has sustained and the possibility of reparation In the early stage before the onset of evident nephritic symptoms the prognosis is excellent and with prolonged treatment *restitutio ad integram* is the rule

Even in established nephritis with a generalised intense dropsical condition a favourable opinion can be given if the disease has not persisted for too long a period Also with careful treatment signs of altered renal permeability tend to persist long after the patient is clinically cured Whether these cases can be regarded as definitely cured remains to be established

For cases in which the disease has reached the advanced stage be it of the chronic parenchymatous dropsical or of the chronic interstitial type the prognosis is serious but much may still be done to prolong life by stopping or at least checking the evolution of the disease by treating the malaria infection if still active

Treatment —The treatment varies according to the stage the disease has reached

In initial cases with prevalent febrile symptomatology with definite urinary findings but only slight clinical signs of kidney disease the treatment is the same as for chronic malaria Quinine should be given in full doses and a nutritious light diet can be allowed

In cases with established nephritis and dropsical symptoms predominating the same energetic anti malarial treatment

should be instituted along with measures apt to reduce the œdema urea is the most useful drug

The question of diet is important as a good nutrition is essential for the successful treatment of the primary malarial disease We have seen that the great majority of our cases belong to the dropsical type and that uræmic symptoms only appear in the very last stages Blood urea estimation whenever possible should be taken as guide In the past I have had to depend mainly on the urea concentration test and on guarded dietetic experiments I have found that most of these wet cases do well on a fairly varied mixed diet with high protein proportion

In most cases response to treatment is very nearly immediate and in two to four weeks the patient can be discharged feeling and looking well In some instances the condition of the patient appears to remain stationary for two or three weeks in spite of treatment then suddenly improvement begins and progresses rapidly and steadily

In these cured subjects the urine remains abnormal albumin continues to be present often in considerable degree but the sediment disappears and the urea concentration and diastatic tests give normal readings Such a condition persists for a long time I have had some cases under observation for over two years they have enjoyed good health taking quinine more or less regularly but their urine still shows from a trace to 3 or 4 per mille of albumin

It is evident that many of the cases of high persistent albuminuria which I have described as common among labourers examined for employment belong to this type *i e* they represent the residue of a remote malarial nephritis Such a hypothesis corresponds to the histories I have collected from these subjects most of whom as we have seen suffered from persistent intermittent fevers followed by œdema in the upper reaches of the Mazaruni river

The treatment of cases of old standing of the wet

chronic interstitial type is much less satisfactory quinine treatment may help to check the progress of the disease if the original malarial infection is still active otherwise it is of little avail The general and current treatment of Bright s disease is required and can only tend to reduce discomfort and defer an inevitable fatal termination

Prevention—We now possess sufficient information to place the question of the prevention of endemic nephritis in British Guiana on a solid base

The disease is *doubly preventable*

(1) It is absolutely preventable in the same degree and by the same means as malaria fever The reduction or eradication of malaria in British Guiana would automatically lead to the reduction or disappearance of endemic nephritis

(2) It is equally preventable by the prevention of chronic untreated relapsing malaria where malarial infection occurs and is frequent

Some important data are now at our disposal for the evaluation of the risk incurred by the individual malarial patient of developing kidney disease in British Guiana

In *P falciparum* infections the risk is nil

In *P vivax* infections nephritis has been found in 4 ?3 per cent of cases

In *P malariæ* infections no less than 48 57 per cent of cases were affected with nephritis

The condition *sine qua non* for the appearance of nephritis is a chronic long drawn infection characterised more by persistence than by intensity The so called low or internal fevers are of importance

No cases of nephritis have been observed in treated cases of chronic relapsing malaria even if the treatment has been irregular and inadequate to bring about a cure but just sufficient to keep the disease under fair control

Though as I have repeatedly stated my statistical figures referring to *P malariæ* need revision this form being in reality much more common than would appear the

enormous tendency of this parasite to cause kidney disease is impressive

It is evident that a competent microscopic diagnosis of the particular form of malaria infection must constitute the base for the prevention of Bright s disease in the individual and in the community

In cases of malignant tertian the danger of chronic nephritis need not be considered

In cases of benign tertian the danger is relatively small and only related to ultra chronic untreated forms

In cases showing *I malariæ* infection the danger is serious I should say nearly specific and the patient should be warned and instructed accordingly

What applies to the individuals applies to the community The determination of the relative incidence of the various malarial parasites in any particular region or in any one particular outbreak of malaria will furnish a reliable base for forecasting the amount of kidney disease which may be expected to follow at a distance of two or three years [1]

Measures which are curative for malaria are preventive as far as Bright s disease is concerned

A Synoptic Review of the Principal Diseases other than Malaria occurring in the Demerara River District in Relation to the Etiology of Chronic Nephritis

The following notes are based on the records of the in and out patient department of the Mackenzie Hospital during the seven years period 19.3 to 19.9

[1] I ha m nt ned lsewh re that d ing th height of th 19 6ep l m Dr O rd f th B itish Gu ana G nt Med al S rv and my lf t a lled th wh l l gth of th nhabited po t n of th Demer a r n est gat g th d ase

I llected many hun treds f blood films only preliminary x minat n was d n t th Ma k nz Hosp t l w tained th film Th unexpected frequ n y of *I I mar* w not d by u b th Unfort nately I hav n rd f th a t al ur l n f th ous p rasite Th film w re tak n by Dr O zard f r furth n estig t n

H se ous illness and d ath prevented him from e r writ ng his repo t Th l at l m t rial ll eted was not utilised Of wh t interest it w uld have been i n w pp rent

Parasitic Diseases

NEMATODE INTESTINAL HELMINTHIC INFECTIONS —The general rate of infection with intestinal nematodes among our cases of nephritis was 70 per cent as regards the individual species ascaris 12 per cent hookworm 60 per cent whip worm 18 per cent strongyloids 4 per cent In no case were the ova abundant or did treatment demonstrate a high infestation

These findings are somewhat lower than the averages for the district which I found in 1923 and the figures given by Haslam and Ozzard for the Pomeroon The height of helminthic infection in the district and of hookworm in particular has without doubt increased during the past years under the influence of repeated campaigns I am referring more to the intensity of infestation than to its diffusion

All the West Indian islanders working for the company received carbon tetrachloride treatment at the time of their engagement In the greater part of the children below three years helminthiasis was not present

FILARIASIS —22 9 per cent of our cases were infected with *Filariæ* 14 5 per cent with *F bancrofti* 8 4 per cent with *F ozzardi*

The average rate of filarial infection among 3 754 patients admitted to the Mackenzie Hospital for all diseases was 16 per cent

PROTOZOAL INFECTIONS

AMŒBIC DYSENTERY is relatively uncommon in the district Not more than ten or twelve cases are seen each year

INTESTINAL FLAGELLATE infections are common (Giardia Trichomonas and Chilomastix) usually associated with intermittent chronic diarrhœa

BALANTIDIUM COLI was noted on one occasion None of these conditions appear to have the slightest relation to chronic nephritis

Acute Infective Bacterial Diseases

SCARLET FEVER measles smallpox alastrim and varicella have never been recorded No case of typical streptococcal sore throat has occurred

DIPHTHERIA has appeared only on a few occasions with sporadic cases

EPIDEMIC PAROTITIS accounts for a few cases every year

LOBAR PNEUMONIA is encountered but is not common

BRONCHO PNEUMONIA is frequent in old East Indians and as a secondary condition in chronic malaria nephritis and paratyphoid

BACILLARY DYSENTERY —Severe and typical cases are rare mild dysenteric syndromes are common but usually associated with malaria they clear up rapidly with plain quinine

TYPHOID —*Bact typhosum* infection is fairly common eight or nine cases are admitted every year

PARATYPHOID A AND B —Have not been observed

None of the preceding diseases have ever occurred with sufficient frequency to render any possibility of an etiological relation between them and nephritis at all likely

Paratyphoid C is the most important of the enteric group it is endemic in the district it appeared in epidemic form during the latter months of 1926 and the early part of 1927

On the relation between the epidemiology of this disease and malaria I have reported elsewhere

This disease deserves special consideration for the following reasons a serious epidemic of paratyphoid C (without doubt affecting some hundreds) coincided with the 1926 malaria epidemic in a series of ninety two cases albuminuria was present in no less than 60 per cent during the course of the fever

In spite of these coincidences I believe that paratyphoid C

can be exonerated from any important part in the etiology of endemic nephritis on the following grounds —

(1) Of the numerous cases of paratyphoid C which recovered and which I have had under observation for three years only one developed nephritis The patient a child of two years and five months was admitted for a double infection of B T malaria and paratyphoid C in November 1926 She was repeatedly seen since as an out patient for persisting relapsing chronic B T malaria In June 1928 she was admitted with fever and dropsical symptoms with heavy albuminuria

(2) In twenty cases of chronic nephritis in which a Widal test was carried out with T A B and C emulsions the result was uniformly negative Identical results were registered by the vital or cultural method Control subjects who *suffered from paratyphoid C at the end of 1926 still* gave evident agglutination in dilutions of 1 100 to 1 400 and over two and a half years after being discharged from hospital

PYOGENIC INFECTIONS —*Staphylococcal and streptococcal* suppurative infections of all forms are very frequent abscesses phlegmons carbuncles lymphangitis adenitis etc etc The nature of these diseases is such that their occurrence can easily be traced in the history of a patient and signs of their passage in the form of scars detected

Suppuration was by no means a prominent condition in the history of our nephritic patients It could be definitely excluded in the adult Negro labourers we have had under observation for years and in the great majority of young little more than breast fed children who represent a high proportion of our cases

GONOCOCCAL INFECTION —This is extremely widespread in the adult population It finds little place in the pathology of infancy and early childhood it is in these ages that nephritis prevails

SYPHILIS —For the serological diagnosis of syphilis the

Meinicke flocculation reaction has been used complement fixation by Hecht s technique has been carried out as a parallel test but owing to the very low titre of complement in the unheated sera of some of the races this reaction gives a high percentage of ambiguous readings through lack of hemolysis in the control tube

In nephritis the percentage of positive readings was 18 7 per cent the two reactions giving concordant results

In a control series of 900 Meinicke reactions carried out on all patients admitted to Mackenzie Hospital the rate of positive reactions was 13 " per cent In a series of "90 reactions the Hecht test gave the following readings positive 10 9 per cent ambiguous 14 1 per cent

Neither the antecedents nor the physical examination of the patients gave any more definite evidence pointing to an undue prevalence of specific infection among nephritic cases

YAWS —This disease is common in the remote histories of many of the islanders Among the natives of the Demerara river it is now very rare I have observed only three cases in seven years

CHRONIC TOXIC PROCESSES — Alcoholism is decidedly rare and could scarcely be incriminated in the numerous infantile cases

The natives are not addicted to any special drug habit or any other special practice which might lead to chronic poisoning

DIET —I have purposely given an outline of the native diet in the introductory section (p 15) on the epidemiology of malaria in the interior of British Guiana

The different habits and temperaments of the various races must be kept in mind the Negro over eats himself whenever he can afford it the East Indian starves himself as he builds up his banking account and covers his women folk with gold and silver ornaments

We have seen that nephritis has presented a real epidemic

wave during the years 1927 1928 1929 following the 1926 epidemic of malaria A similar though small rise was noted in 1925 after the small malaria outbreak of 1924 In both instances these rises corresponded to a parallel increase in the incidence of blackwater a typical manifestation of chronic malaria

Few things are more uniform or unvaried than the diet conditions of the natives from year to year

In the case of the Aboriginal Indians and of the Bovianders whose diet depends entirely on self produced and self procured foodstuffs a serious malaria epidemic would tend to alter not only the amount of food available but also the normal balance of the diet But it is difficult to see how malaria could affect the diet of the wage earning Negro who counts on the shops and stores exclusively for the purchase of his food

The equal incidence of the disease among the different races in spite of their different dietetic habits and its tendency to occur in epidemic waves stand against any theory which should invoke food deficiency as an etiological factor in endemic nephritis

From the well fed good food loving Negro to the half starved rice eating Coolie from the Chinese or Syrian shop keeper to the frugal Buck Indian hunter with his cassava and peppers Bright s disease takes its toll with strict impartiality wherever chronic untreated malaria holds the field

Conclusions

The present investigation is based on data collected from the study of 102 cases of chronic nephritis and their relation to other diseases and conditions as seen on the mid Demerara river British Guiana during the seven years period 1923 to 1929

The limitation of the field of investigation the strict medical control exercised over an important section of the

mining population personal knowledge of the antecedents of most of the patients systematic hospital records and exact information on the general conditions of disease sanitation living etc among the natives of the district have all contributed to facilitate and circumscribe the problem

Epidemiology —During seven years observation though a few sporadic cases have occurred at all times the incidence of nephritis in the district has shown some very important fluctuations

Important malarial outbreaks are followed by an important increase in the incidence of chronic nephritis This increase is proportionate to the entity of the malaria epidemic

The rise in the nephritis curve is synchronous with that of blackwater fever

In British Guiana blackwater appears immediately in the train of a malarial epidemic it reaches its maximum of incidence nine months later and tends to disappear within little more than a year Nephritis follows a similar curve but as a chronic disease it tends to establish itself more slowly and to persist over a much longer period Its maximum incidence has been noted in the second year following a malarial epidemic

It is evident that the consequences of chronic nephritis are far reaching and though the onset of an epidemic wave is evident its fall and cessation are gradual and indefinite

Among the Macussi and Wapisiana Indians of the Rupununi savannahs in the far interior malaria is reported to be frequent but exclusively among individuals who have travelled through the forest districts to the coast or have been engaged in balata bleeding on the upper Essequebo The termination of such fevers with a rapidly fatal dropsical syndrome is common

Parasitology —Malaria parasites were found in the blood of sixty one out of eighty seven patients examined who were suffering from chronic nephritis *i e* in 70 per cent of cases

During the same period the incidence of parasites in the

blood of plain clinically diagnosed malaria cases examined by the same technique was 40 per cent

In no case was *P falciparum* found as a pure infection in the blood of nephritic patients On two occasions it was found as a double infection with *P vivax*

During the same period *P falciparum* accounted for 15 7 per cent of malarial infections *in the district*

P vivax was found forty three times in sixty one positive bloods from nephritic cases (70 per cent)

On a series of 1 247 positive blood examinations in fever patients *P vivax* accounted for 1 016 cases (81 4 per cent) of these forty three or 4 23 per cent referred to cases of chronic nephritis

P malariæ was found seventeen times on sixty one positive bloods from nephritic patients (30 per cent)

On a series of 1 247 positive blood examinations in malaria *P malariæ* accounted for only thirty five cases (2 9 per cent) of these no less than seventeen 48 57 per cent referred to cases of chronic nephritis

The relation between nephritis and the various kinds of malarial parasites shown in Nos 6 7 8 and 9 cannot be accidental chronic nephritis is found exclusively associated with the benign forms of malaria which are notorious for *their great tendency to chronicisation and recurrence* It appears nearly specifically related to *P malariæ* a relatively rare form of infection among uncomplicated cases of malaria

Statistical—The incidence of nephritis is highest among the permanent residents of the malarial hyper endemic river areas (65 6 per cent of cases)

Nephritis occurs among all races with approximately equal frequence in our series the East Indians appear the most liable and the Negroes the least

Demerarian Negroes and recently immigrated Negroes from the West Indian Islands are equally subject to the disease

Nephritis is prevalently a disease of children (54 per cent

of cases amongst the Boyianders) It rarely develops in infants below two years of age (Necessity of prolonged action of malarial infection on the kidney)

Both sexes are liable to the disease whereas in child hood the sex distribution is equal among adults nephritis is much less common in females than in males (Influence of exposure)

From what has been said in Nos 5 11 12 13 and 14 the epidemiological characters of blackwater and chronic nephritis appear to coincide *The only point in which they differ* concerns the susceptibility of the Negro race to nephritis in contrast to its distinct immunity to hæmoglobinuria

This difference is easily explained given the fundamental difference in the pathogenesis of the two diseases in spite of the identity of their primary etiological factor

Albuminuria and Malarial Nephritis —Albuminuria has been found in 25 per cent of 550 cases of malaria giving a positive blood examination The incidence of albuminuria varies in different forms of malaria infections 20 per cent subtertian 5 per cent in benign tertian 46 per cent in quartan malaria

In benign tertian and quartan malaria albuminuria is rare in recent and in more or less regularly treated chronic infections its frequency increases progressively with the duration of the infection and its tendency to relapse

In untreated chronic relapsing benign tertian and quartan malaria the sequence fever with normal urine fever with intermittent albuminuria fever with persistent albuminuria cast *leukocytes and renal elements in the sediment* fever and sub chronic nephritis with dropsical symptoms chronic parenchymatous or chronic interstitial nephritis has been repeatedly witnessed step by step in individual patients

Albuminuria in the benign malaria infections represents the first link of a chain leading to chronic parenchymatous or chronic interstitial nephritis if the malarial infection is not naturally overcome or appropriately treated

Clinical—In our series of 102 patients all cases gave a history of persistent fever 80 per cent presenting a temperature at the time of admission The fever is intermittent and usually of the quotidian type tertian and quartan fevers are frequent

No case of acute nephritis has been observed Red cells are exceptional and always very scarce in the sediment

The prevalent forms seen during the first three years following the malaria epidemic were characterised by extensive œdemas and serous peritoneal effusion Uræmic symptoms were exceptional Cardio-vascular alterations did not occur

In other cases the characters were those of chronic nephritis with increased blood pressure and hypertrophy of the heart

Chronic interstitial nephritis being an incurable disease of long duration is liable to outlive the primary malarial infection which determined it

Prognosis—It is evident that in most old standing cases of malarial nephritis search for parasites in the blood may be negative

The primary etiological factor being known and curable the prognosis is based essentially on the degree of damage which the kidney has already sustained The duration and form of the malarial infection is an important element

Treatment—Varies with the stage of evolution of the kidney disease

Prolonged energetic plain anti malarial treatment is sufficient in early cases In cases of established nephritis with malaria still active brilliant results follow the administration of quinine in full doses along with the routine treatment of nephritis

A high protein diet is usually well tolerated and beneficial in the œdematous cases In old standing cases the malarial infection may have disappeared quinine may be given but the treatment remains essentially the one of chronic nephritis from any other cause The disease is incurable

Prevention—Malarial nephritis is preventable in *the healthy individual* by the prevention of malaria in *the infected individual* by rational malaria treatment

In the community it is radically preventable through the eradication of malaria When this is not possible *it is equally preventable by rational treatment of the infected under the intelligent control and direction of systematic microscopic examination*

The presence or prevalence of *P malariæ* is a danger to the individual and a menace to the community

Physician and sanitarian must join efforts and may equally contribute to the fight for the control of endemic or malarial nephritis in British Guiana for the prevention of some 1 000 deaths a year and of an incalcuable amount of disea e misery and of finan ial loss

PART IV

A SHORT REVIEW OF THE LITERATURE ON MALARIAL ALBUMINURIA AND NEPHRITIS

Malarial Nephritis as a Nosological Entity Its Clinical Forms in Relation to the Various Species of Malaria Parasites

The dropsies that occur are very enormous and very fatal for in the summer there are epidemics of dysentery diarrhoea and long quartan fevers which diseases when prolonged cause such constitutions as I have described to develop dropsies that result in death

There was danger lest death should occur among young children and women and least of all among old people and that the survivors should lapse into quartan fevers and from the quartans into dropsies

Hippocrates

THE literature concerning the renal function and its alterations in malaria fever is relatively scarce

The most important works are those of the Roman School published in the last years of the past century

The findings of these earlier workers have since been repeatedly quoted while the new contributions and statistics which have at various times been published have added but little to our knowledge

An analysis of the literature demonstrates a remarkable discrepancy among the findings of the various authors working in widely different countries The interpretation of such results is all the more difficult as the majority of the available statistics are so incomplete as not to furnish the essential data required for a general comparative study of malarial renal disturbances and of the factors which determine or influence them It is in fact necessary to know

not only the percentage of albuminuria or nephritis among malaria cases but also the relation of these conditions to the various forms of malaria infection to the duration of the disease to its intensity the relation to age sex race the general clinical and epidemiological character of malaria in the particular region etc

Hirsch (1869) writes The frequently expressed opinion that *Morbus Brightii* should be a frequent complication of malaria fever or symptom of cachexia requires limitation The rarity of nephritis in Southern Benguela and in Brazil both of which are highly malarial countries testifies at least against the generalisation of such an opinion

In Europe Rosenstein (1858) was the first to draw attention to the marked variation in the frequency of nephritis in malaria in different epidemics and localities

The same author (1896) in a series of 16 cases of nephritis found 3 per cent which appeared to be of malarial origin these he classified in three groups (*a*) renal attacks accompanying plain intermittent fevers characterised by the absence of the sweating stage (*b*) renal attacks appearing in malarial patients returning to their occupations after a fever attack (*c*) renal attacks appearing in individuals who have suffered from obstinate persistent fevers especially if untreated

All the cases presented œdema the characters of the urine were those associated with large white kidney Though *acute nephritis* may occur in cases in which the sweating stage is absent the author insists particularly on chronic nephriti

Quinin cured both fever and nephritis

No death was registered and no case evolved into a progressive chronic disease The duration of the renal symptoms was from fourteen days to four months

Much stress is laid on the variation in frequence of nephritis in individual epidemics and in different localities

Heidenhain is quoted as having studied a series of malarial

epidemics in all nephritis was conspicuous for its absence only in the last nearly every case presented secondary renal symptoms

Bartels in Germany *considers malaria as the* most frequent cause of nephritis after chronic suppuration He registered a large number of cases among labourers admitted to hospitals in the Elbe valley and along the coast of the North Sea from the swampy lowlands of Schleswig Holstein This serious renal disease appeared during the course of long standing intermittent fevers But similar cases were also admitted from the Baltic coast and the continental part of the province where malaria was rare

Senator (1896) reports having seen nephritis in malarial subjects

In Rome Rem Picci in a series of very well documented papers and monographs studied the urinary secretion and its alterations in malarial patients from the Roman *Campagna during the period 1891 to 1898 During this* eight year period he collected eighty cases ranging from plain albuminuria to established nephritis Although admitting that a considerable number of cases with kidney altera tions escaped observation considering that at the time about 50 per cent of the 6 000 patients admitted annually to the Santo Spirito hospital were affected with malaria the author concludes that around Rome renal lesions are a rare com plication of malaria

From a study of the statistical records concerning the mortality from renal diseases and the incidence of malaria among the patients admitted in various hospitals situated both in malarial and non malarial provinces in Italy Rem Picci and Silva both obtained contradictory results

For the detection of albuminuria and of the early nephritic cases Rem Picci found it necessary to resort to the systematic examination of the urine in all patients admitted for malaria *A considerable number* of cases were thus observed in which the etiological relation between malaria and nephritis

could not be doubted in others this relation was less clear on this subject the author writes as follows having once admitted on the base of reliable observation as certain the malarial origin of some cases of renal disease I am obliged to ascribe to this same cause all those cases in which malarial infection is conspicuous in the history and is intimately connected with the onset and evolution of the nephritic process

One might be reproached with hyper criticism if one denied such an etiological relation at least ir accordance with the system of reasoning which we are used to follow in the study of pathology With too severe an exclusivism also other toxic processes currently regarded as of etiological importance in the causation of chronic nephritis such as syphilis gout alcoholism would have to be put aside In fact in individual instances even with greater difficulty than in our malarial cases can the etiological relation to such conditions be exactly established

Rem Pi ci classifies the cases he observed as follows —

Malarial Albuminuria —(*a*) Febrile occurring during the fever paroxysm incidence 6 per cent

(*b*) Post malarial occurring two to four days after the fall of the fever frequently accompanied by polyuria incidence 2 per cent

(*c*) In cachectic cases a rare form

Malarial Nephritis —(*a*) Acute nephritis It may occur during a fever attack or follow it two forms (1) slight (2) hæmorrhagic

(*b*) Sub acute nephritis The time of onset of the kidney symptoms is indefinite owing to the latent and subtle nature of the process

(*c*) Chronic nephritis Derives from the evolution of an untreated acute process Frequently the disease is so gradual as to become apparent only when the chronic stage has been reached

(1) Chronic parenchymatous nephritis

(2) Chronic interstitial nephritis

Amyloid Degeneration of the Kidney

The limit between albuminuria and nephritis is naturally not defined the author insists on the importance of repeated attacks of malaria both as the primary cause of renal disease and as *an aggravating influence once* kidney lesions have got established

As to the relation of the various forms to each other he writes It is likely that malaria which in a first attack had no influence on the kidney should at a latter date produce persisting albuminuria which especially if neglected may be the starting point of a permanent renal lesion

As regards the relation of renal disease to the various kinds of malaria parasites Rem Picci found them commonest in benign tertian and quartan infections and rare in subtertian and pernicious cases in spite of diligent search Nephritis was commonest at the end of the autumn and *beginning of winter it was more frequent in young subjects* It is the recognised opinion of the medical practitioners of the Pontine Marshes that malarial nephritis is less rare in children than in adults Maggiora in Milan has recently confirmed this contention

Marchiafava and Bignami (190-) mainly *follow Rem* Picci s findings The following statement is of interest

It *is* worthy of note that polyuria is observed with greater frequency in patients affected with benign tertian and quartan rather than in those suffering from æstivo-autumnal infections This difference appears to be related to the specific form of the fever and not to accidental circumstances or *to the season in which these various fevers tend to prevail*

Concerning the pathogenesis of renal affections in malaria these authors are somewhat reserved Any statement regarding the pathogenesis of the renal lesions observed in malarial infections can only be given as a hypothesis do we perhaps know by what process *nephritis develops in* scarlet fever ? The knowledge of the specific organism which causes malaria at least for the present has thrown no light

on this problem In pernicious cases one finds only very few parasites in the vessels of the kidney on the contrary degenerative changes in the epithelial cells are serious and may go as far as actual necrosis From such findings one can conclude with Bignami that these lesions are not in relation to the clogging of the renal capillaries by the malarial parasites but to some toxic substance which the blood stream brings to the kidney for elimination The increase in the toxicity of the urine would favour such a contention As to the nature of the toxic substance capable of producing renal alterations nothing can be said Are we in the presence of specific toxins elaborated by the malarial parasites or of the toxic products resulting from the destruction of the parasites of the red blood corpuscles of the phagocytes or from the altered general metabolism? And if toxins are always produced why are renal complications rare? Which are the intermediary factors which are capable of rendering the kidney susceptible to the action of these toxins?

Remlinger Roque and Lemoine found an increase in the toxicity of the urine after a malarial paroxysm Boltazzi and Lensuti found it highest during the apyrexial period and noted a tendency in it to increase with the repetition of the febrile attacks

According to Ascoli (1915) both mechanical circulating alterations and toxic processes play a part in the causation of renal lesions in the course of malarial infections these may range from slight transitory disturbances to real nephritis He explains the marked discrepancies among the statistics given by different authors by considering the wide differences in the general condition of living of the patients examined habits dietary prevalence of one or the other kind of malarial parasite duration of infection number of relapses intensity of infection method of examination etc He insists on the importance of the individual factor

On albuminuria in malaria Ascoli concludes as follows —

(1) The incidence of albuminuria in malarial cases varies within wide limits from one region to another

(2) Albuminuria is much more frequent in cachexia than in fever attacks

(3) It is more frequent in malignant malaria

(4) It is more common in young subjects

(5) Though it is permissible to regard albuminuria as bordering on nephritis the actual passage of cases of plain albuminuria into nephritis has not received the confirmation of clinical observation

(6) Orthostatic albuminuria may follow a malarial attack

It is important to note that according to this author (mainly on the base of Roman experience and of Thayer s statistics—*vide infra*) three quarters of the cases of nephritis in malaria present blood in the urine Uræmic symptoms are rare Clinically he classifies cases as *acute* and *chronic* of the latter he describes two forms *slight* and *grave* both of which are characterised by hæmaturia

Chronic cases can present the type of the large white or variegated kidney and sometimes of the secondarily con tracted kidney

In North America in 1884 Atkinson drew attention to albuminuria and nephritis of malarial origin giving a long list of references particularly by American authors

Thayer and Hewetson s accurate work (1895) has been widely quoted on 335 cases of malaria these authors found 133 cases of albuminuria and four of nephritis in another *series of 300 cases albuminuria was present in 50 per cent*

In 1909 Thayer in Baltimore found albuminuria present in 38 6 per cent of 352 cases of B T and quartan malaria and in 58 per cent in a series of 165 cases of malignant tertian Other American authors have confirmed these findings (Craig 1909 Deaderick 1913 Henson 1913)

In the tropics numerous statistics have been made

Specifications as to the kind of malaria *parasite present* the influence of acute or chronic infections etc are lacking *so that much of the* value of these observations is lost It is evident that routine examination of both urine and blood in all malaria cases has only very rarely been carried

out This is hardly surprising when one considers how rarely even simple blood examination is performed in most malarial countries and how deficient are the records concerning the local incidence of the various malaria parasites It may safely be said that reliable information of such nature is more the exception than the rule

In Panama Bates (1913) recorded albuminuria in 42 per cent in a series of 200 cases Deeks (1910) states that nephritis was the most frequent complication of malaria in the Canal Zone usually disappearing after convalescence but sometimes persisting and ending fatally

In the Philippines Willets (1914) found albuminuria in 33 3 per cent of 348 cases In Senegal Marchoux registered it in 97 5 per cent of forty cases and Holmes à Court in 48 9 per cent of thirty five West African cases

In India James (1922) writes Temporary albuminuria is frequent especially towards the end of the febrile paroxysm Rogers on the contrary states that the urine very rarely shows albumin or other changes in uncomplicated cases Sinton and Lal (1929) have reported on albuminuria in malaria and its occurrence during quinine and alkali treatment among prisoners in Lahore They found it present in 17 2 per cent of fifty seven benign tertian and in 14 per cent of 410 malignant tertian cases They mention the following conditions which may have contributed to determine the remarkable variations recorded by different authors in the incidence of albuminuria

(*a*) The possibility of selected populations (*b*) the dosage of quinine and the mode of administration (*c*) the number of days on which the urine was examined for albuminuria (*d*) the diet of the patients (*e*) climatic conditions (*f*) normal incidence of albuminuria

Of very particular interest is a short note by J Tertius Clark on nephritis and quartan malaria in the Federated Malay States It is unfortunate that so important an observation should not have been completed by a fully documented study

We read I believe that the occurrence of œdema in the tropics of such a nature as to make one think of parenchymatous nephritis is a reason for making a search for quartan malarial parasites imperative sixty two cases which in the ordinary course of events would have been diagnosed as nephritis came under my care in the Ipoh hospital their symptoms were *weakness difficulty in breathing* and swelling Of these sixty two cases only five complained of fever

The point I want to lay stress on is that in these five cases only would the blood ordinarily have been examined for malaria parasites the remaining fifty seven all of which from the record shown had albuminuria would have been treated by ordinary remedies for nephritis whereas thirty two out of fifty seven that is 56 per cent had malarial parasites in their blood and obviously the correct treatment was quinine *And further* *Every medical man knows* that given the malarial parasite he may find albuminuria but he does not know that given the albuminuria without any fever he may find malarial parasites in over 50 per cent of the cases and that of this 50 per cent almost 100 per cent are quartan

In a table sixty two cases are recorded showing albuminuria and œdema Only five had fever thirty two had malaria parasites and of these twenty nine were *P malariæ* Figures relating to the incidence of *P malariæ* in relation to other infections in Ipoh districts are not given

The author regards syphilis as another important cause of nephritis

The association of nephritis with quartan malaria has been observed in sporadic cases by many workers Marchiafava and Bignami gave the autopsy findings of a case of quartan malaria which died of nephritis the association of the two diseases was regarded as accidental

Malcolm Watson in the Federated Malay States reports on a series of eighty three cases of quartan *twenty seven* of which presented œdema and six albuminuria he writes

In some (cases) the brunt of the disease appears to fall on the kidney and parenchymatous nephritis ensues

Swan in 1909 described a case of nephritis with a small granular kidney in a quartan malaria patient from Jamaica Bass reported on a similar case

More recently Manson Bahr and Maybury (1927) have reported on two cases of nephritis associated with quartan malaria observed in London The first came from India the second from the Federated Malay States both had extensive œdema and 1 0 and 1 5 per cent albuminuria respectively Both cases cleared up after a month s energetic quinine treatment the improvement of the kidney condition being parallel to the effect of the treatment on the blood parasites The authors suggest that quartan malaria may play an important *rôl* in the etiology of tropical nephritis Surbek in 1) has reported on four cases of nephritis in native children suffering from severe untreated quartan infections in Sumatra

In Ceylon S I James and Gunesekara (1913) have reported the following incidence of the various malaria parasites *P malariæ* 71 per cent *P vivax* 18 per cent *P falciparum* 10 per cent In the same island but from another area Bahr (1913) also found *P malariæ* in predominance

Under the somewhat elastic term of dropsy we find 2 580 and 1 986 deaths registered in the years 19 4 and 19 5 respectively in Ceylon the number of deaths from all causes for 19 5 being 11" 515 The number of admissions and deaths for nephritis in the Ceylon hospitals for the years 19 5 19 6 and 1927 were the following —

19 5	Cases	54	Deaths	5 4
1926		2 986		510
1927		00		519

These figures seem to point to a high proportion of cases of kidney disease in the colony further studies to establish the possible relation between quartan malaria and dropsy would be of interest

As regards the *post mortem* findings in the kidney of fatal malarial cases and malarial nephritis in particular reference should be made to Marchiafava s and Bignami s classical studies and to Kelsch and Kiener s work

Marchiafava and Bignami (1902) described a typical acute glomerular nephritis associated with quartan A similar case is mentioned by Swan (1909) and another by Bass (1909)

In Georgetown Daniels (1897) found 228 cases with renal lesions in a series of 926 consecutive malarial autopsies (25 per cent)

From a review of the literature and the result of my own observations in British Guiana I believe that the apparently contrasting findings of the various authors who have worked on malarial albuminuria and nephritis can be easily reconciled malarial nephritis appears as a well defined nosological entity presenting special forms in relation to the different kinds of malarial infection The variations found from one country to another are simply the expression of the different parasitological conditions and of the different environment which exercise so important an influence on the evolution of malaria in the mass and in the individual Not much is known as to the nature of malaria toxins or their mode of action

The following facts however can be taken as practically established —

(1) All three kinds of malaria parasites either directly or indirectly elaborate one or more toxic substances which have a deleterious action on the tissues of the organism

(2) The nature amount and mode of action of such toxins is different according to the species of malaria parasite

(3) Clinical and anatomical findings authorise the presumption that the toxins produced by *P falciparum* are more powerful and more violent in their mode of action

This infection has least tendency to chronicity and relapse and the toxins act more by mass than by cumulative process *P malariæ* of all the malarial parasites is the mildest as far as intensity of the febrile reaction it determines is con

cerned it is also the most persistent and ineradicable and the most constantly active as is evidenced by its nearly continuous presence in the peripheral blood of infected subjects *even when apparently in good health*

Definite data from the Federated Malay States and British Guiana demonstrate the existence of very serious kidney alterations as a consequence of these prolonged infections The toxins elaborated by *P malariæ* act by a slow continued cumulative process

(4) *P vivax* presents intermediary characters between the two *preceding Its toxin works partly by mass action* and partly by slow continued cumulative process

(5) The toxins elaborated by all the three kinds of malaria parasites act on the tissues of the kidney and are capable of determining serious disturbances in the urinary function

(6) The anatomical and clinical characters of these alterations and their course are in relation to the mode of action of the specific toxins *acute* and due to *mass action* in the case of *P falciparum* infection *chronic* and due to *continued cumulative action* in the case of benign tertian and quartan infection

(7) When malignant malaria prevail and is severe albuminuria is very frequent in the symptomatology of acute malarial attacks (Marchoux in Senegal Thayer in Baltimore) acute hæmorrhagic nephritis is not rare (Thayer Deeks and other American observers)

Nephritis caused by parasitic embolism of the renal vessels has been described (Ewing) but is exceptional

(8) In countries (equatorial climates British Guiana Federated Malay States Sumatra probably Ceylon) *where* benign tertian and quartan prevail and climatic and other conditions are such as to further a prolonged *continued* unhindered activity of chronic malarial infections albuminuria is common acute nephritis is exceptional *sub chronic and chronic parenchymatous and chronic interstitial* nephritis are common Their incidence is proportionate to the incidence of *P malariæ*

(9) In countries where malaria of all forms occurs but

climatic conditions are such as to restrict the active malarial season to only a few months in the year where chronic cases have the benefit of a prolonged respite during the winter months with wide opportunity and facilities for treatment albuminuria is rare nephritis is rarer (Roman Campagna)

(10) The absence of albuminuria and nephritis as a complication of malaria in any given malarial country will probably be found to be in relation to the absence or rarity of *P malariæ* or to the particular conditions of climate and civilisation which are unfavourable to the prolonged untroubled evolution of chronic infections

(11) The different incidence of nephritis and albuminuria in different malarial epidemics reported by many authors (Atkins Heidenheim Ascoli etc) can be easily explained by a variation in the incidence of the various species of malaria parasites

The following table aims at recapitulating in a synoptic form the relations between the various kinds of malaria parasites and malarial albuminuria and malarial nephritis in its various forms which I have described in British Guiana or which have been described by other authors in other ountries

P falciparum Subtertian Malaria

In severe forms ⟶ febrile or post febrile albuminuria ⟶ acute hæmorrhagic nephritis ⟶ possibly but rarely chronic nephritis

Anatomical findings Acute degenerative parenchymatous alterations congestion very rarely parasitic embolism of the renal vessels acute hæmorrhagic glomerular nephritis

P vivax Benign Tertian Malaria

Chronic relapsing untreated B T malaria ⟶ albuminuria⟶sub chronic nephritis⟶chronic parenchymatous nephritis⟶chronic interstitial nephritis

Anatomical findings Early *alterations* probably simply congestive and degenerative⟶large white kidney Secondarily *contracted kidney*

P malariæ Quartan Malaria

Chronic relapsing untreated quartan malaria⟶ albuminuria⟶chronic parenchymatous nephritis⟶ chronic interstitial nephritis

Anatomical findings Early alterations congestive and degenerative⟶large white kidney⟶secondarily contracted kidney

The tendency of *P malariæ* to produce nephritis appears to be ten times greater than that of *P vivax*

Very recently Latini (1929) published some observations on patients admitted for malaria to the Santo Spirito Hospital in Rome during the period 1924-1928. This work is of particular interest as it was carried out in the same hospital where Remlinger made his observations in 1894-1898. Data are therefore available for a comparative study on the incidence in the Roman Campagna of renal disease in malaria patients before and after the introduction of modern means and methods of malaria treatment and control

On 1 470 admissions 347 were classified as benign tertian 56 as subtertian with 16 pernicious forms 4 as quartan 75 as double B T —M T infections 10 as chronic (form of infection not specified) 333 as undetermined

Albuminuria was not d in 10 per cent of benign tertian infections 15 to 18 per cent of subtertian 15 per cent of double B T —M T infections 0 per cent of quartan 10 per cent of chronic forms The amount of protein present was usually very slight Definite signs of renal disease were very rare and practically always associated with *P falciparum* infections Nephritis was found in 0 7 per cent of all cases excluding pernicious forms (16 cases only) In the latter on the contrary renal involvement was frequent being noted in 40 per *cent of cases* Nephritis was in no instance found in association with *P malariæ* but only four cases of such infection were recorded

Only two cases of chronic nephritis were registered the rest presented the type of acute parenchymatous forms usually mild and transitory Many cases would have been overlooked if the laboratory methods had not been employed as a routine

Comparing his findings with those of Remlinger (*vide supra*) Latini writes as follows "We can therefore conclude that the renal diseases which have occurred in malarial patients (from the Roman Campagna) during the last four years presented a much milder and plainer symptomatology than what has been described for the numerous cases recorded during the last years of the past century and that the tendency of such cases to pass into chronic conditions has been greatly reduced And further With the progress of malaria control with the greater facilities for early and efficient quinine-treatment and hospitalisation of patients in suitable hygienic environment kidney diseases of malaria origin as other organic diseases depending from this infection tend to become progressively milder and to acquire a transitory character"

APPENDIX

MALARIAL NEPHRITIS

SOME CLINICAL CASE REPORTS

Endemic Nephritis Clinical Cases

Chronic Quartan Malaria fever—Albuminuria —CASE No 1—L A aged 20 male Race Negro Locality native of Berbice residing at Akyma Demerara river since four months Labourer

History states not to have suffered from fever in his native village He contracted malaria a few weeks after his arrival on the Demerara river

20/1/29 examined for employment returned as fit urine negative for albumin

11/2/29 seen as out patient for malaria fever

-8/3/29 seen as out patient for malaria fever blood positive for large ring forms Urine negative for albumin

13/5/29 admitted to hospital with fever lumbar pain and cough Temperature 101 F Blood positive for *P malariæ* (trophozoits) Stool negative Meinicke and Hecht *reactions negative*

Urine amount passed in twenty four hours 3 400 c c reaction acid gravity 1014 albumin 0 5 per mille urea concentration test 2 diastatic test 20 sediment negative Clinical course with simple quinine treatment fever and albuminuria disappeared on the third day

CASE No 2—B D aged 7 male Race East Indian Locality Christianburg Demerara river

History was healthy up to the age of 5 he contracted

malaria at the end of 1926 and has been sick on and off at very frequent intervals ever since

6/7/27 seen as out patient has suffered from intermittent fever for two weeks passed black urine yesterday blood presents large ring forms Treated with stovarsol gr 1 t d s Three days later quinine hydrochlor gr 1½ t d s was administered but it provoked another attack of hæmoglobinuria

18/7/27 admitted to hospital for blackwater fever

10/12/28 seen as out patient has suffered from intermittent fever for two weeks Blood positive for *P malariæ* (trophozoits) Urine negative for albumin Treatment stovarsol gr 1¼ and quinine hydrochlor gr 1¼ t d s

13/12/28 returns with fever still persisting quinine gr … t d s prescribed the family being warned of the danger of renal complications if the treatment is not carried out and continued for some months

4/1/29 returns with fever the treatment prescribed at the last examination was suspended after a few days the patient has suffered from fever ever since The spleen reaches the umbilical line Blood positive for *P malariæ* (trophozoits in various stages typical band forms) Urine albumin positive 0 5 per mille sediment negative Treatment quinine gr … t d s cod liver oil drach 1 t d s Fever and albuminuria disappear on the fifth day of treatment

Case No 3—B M aged 18 male Race Aboriginal Indian Locality native of Morawannha North west district residing at Bootoba Demerara river Woodcutter

History did not suffer from fever in Morawannha Has suffered from low fever ever since his arrival at Bootoba attacks coming on every two or three days with slight chills Spleen enlarged and painful

15/4/29 admitted to hospital general state of nutrition

good the spleen is palpable at the costal margin and tender anæmia no œdema temperature normal Blood *P malariæ* (trophozoits) *Stool ova of ascaris present* Meinicke reaction positive Urine amount passed in twenty four hours 1 250 c c albumin positive 0 3 per mille *gr* 1 014 *urea concentration test* 1 5 *diastatic* test 10 sediment none Under plain quinine treatment fever and albuminuria cleared up and the patient was discharged *on the fifth day*

Chronic Quartan Malaria fever—Chronic Nephritis—CASE No 4—R A aged 22 male Race Negro Locality native of Saint Lucia B W I residing since six months at Akyma Demerara river Miner

History enjoyed good health in his native island Came to British Guiana in June 1928

17/7/28 physically examined for employment returned fit urine negative for albumin

1/8/28 admitted to hospital suffering from fever since six days Blood positive for large rings Stool positive for hookworm ova Meinicke and Hecht reactions negative Urine contains a trace of albumin Treatment quinine *gr* 10 t d s on the second day *gr* 15 by intramuscular injection On the sixth day carbon tetrachloride M 45 followed by magnesium sulphate Clinical course the temperature rose to 102 F on the second day it fell to normal on the third day The patient was discharged on the seventh day with quinine treatment for ten days His urine was negative for albumin

18/9/28 admitted with a history of fever and head ache since three weeks Temperature normal rising to 103 on the following day Blood negative for malaria parasites (has taken quinine) Urine positive for albumin Treatment quinine gr 10 t d s Clinical course the fever broke on the third day discharged on the fifth day

with treatment for t n days The urine still contains a trace of albumin

3/11/28 admitted with a history of fever at frequent intervals with headache lumb ır pain and cough since two weeks slight ædema of the face and ankles Temperature 102 F Pulse 100 Blood pressure systolic 140 mm Diastolic 85 mm Differential 55 mm Blood *P malariæ* gametes abundant Urine amount passed in twenty four hours 950 c c sp gr 1 010 reaction acid albumin positive 0 5 per mille sediment abundant hyaline granular and epithelial casts few leukocytes no red cells urea concentration test 1 5 diastatic test 6 6 Treatment quinine hydrochlor 10 t d s Diet soft mixed Clinical course the temperature curve presented a typical quartan periodicity it fell to normal on the fifth day The urinary condition remained stationary The patient was discharged and certified unfit for further employment on the fifteenth day receiving treatment for two weeks

11/12/28 reports to be feeling well has had no more fever and wishes to return to work Urine albumin 0 5 per mille sediment hyaline and granular casts and few leukocytes present

15/1/29 has been working as woodcutter since three weeks Feels well has had no fever and no more œdema Urine the albumin has risen to 1 8 per mille sediment hyaline and granular casts and few leukocytes present

CASE No 5 —R A aged . years and 4 months female Race mixed Locality Christianburg Demerara river (Fig 14)

History began to suffer from fever at the age of four months (December 19 6) and has had attacks at very frequent interval ever since

8/3/28 treated as out patient for malaria fever blood not examined

5/4/28 seen as out patient for intermittent fever spleno megaly and œdema of the face and ankles Urine positive for albumin 1 per mille sediment hyaline and granular casts Treatment quinine gr 3 t d s for three weeks



FIG 14 —Chronic Nephritis in a female child of mixed race a two years and four months suffering from a chronic quartan malaria infection of twenty four months standing

theobromine gr 1½ t d s With recommendation to repeat this treatment continuing it for several months After one week of treatment the fever and œdema had disappeared the treatment was not repeated as prescribed

12/12/28 the child is reported to have enjoyed fair health up to the end of November seen as out patient

fever returned one week ago with generalised œdema General condition of nutrition poor the face is swollen the eyes nearly closed the abdomen is enormously distended the genitals legs and feet are œdematous The patient is very dyspnœic and must keep the sitting position The spleen passes the costal margin by two inches Blood positive for *P malariæ* in all developmental stages very abundant Stool negative Urine albumin present 8 per mille sediment hyaline granular and epithelial casts leukocytes abundant The parents refusing to leave the child in hospital the same treatment as above is prescribed

2-/12/18 admitted to hospital condition aggravated the treatment having been carried out irregularly Weight 24 lbs Temperature 100 F Blood positive for *P malariæ* Urine albumin 10 per mille sediment as above gr 1010 diastatic test 6 6 Treatment quinine hydrochlor gr 4 t d s theobromine gr 1½ t d s mist alba drach 1 mane Diet milk Clinical course the temperature fell to normal on the second day but rose to 99 F every afternoon till the eleventh day from the ninth day the œdema and ascites began to reduce and with them the amount of albumin The patient was discharged on March 31st 1921 all signs of œdema having disappeared the albuminuria was reduced to 0 9 per mille the diastatic test had risen to 10 the sediment was very scanty with very few casts the weight had fallen to 17 lb

CASE No 6—H A aged 39 male Race mixed Locality Christianburg Demerara river Woodcutter

History states to have been healthy up to the end of 1916 when he contracted malaria during the epidemic He has suffered continual relapses ever since During the last six months he is not aware of having actually had fever but has often felt chilly and has suffered from lumbar pain

and dizziness, his urine is always highly coloured he has been unable to work for many months

27/12/28 *admitted to hospital*, *general state of* nutrition good anæmic with characteristic terreous complexion the spleen is not palpable the feet legs and abdominal wall are œdematous there is a small amount of free fluid *in the peritoneal cavity* *There is some hypertrophy* of the heart the apex beat being felt half inch outside the nipple line Lungs normal Temperature 99 3 F Blood pressure systolic 170 diastolic 90 differential 80 mm Blood positive for *P malariæ* in all developmental stages Stool positive for ova of hookworm and whip worm Meinicke and Hecht reactions negative Widal test with T A B C emulsions negative Urine albumin positive 2 per mille gr 1010 reaction acid sediment hyaline granular and epithelial casts abundant few leukocytes no red cells urea concentration test 1 5 diastatic test 5 Treatment quinine hydrochlor gr 10 t d s On the seventh day carbon tetrachloride M 30 followed by a full dose of mag sulph (passed twenty one worms) Clinical course the temperature fell to normal on the second day the œdema and general condition remained stationary On the twelfth day the temperature rose suddenly to 102 F with cough and sharp thoracic pain severe dyspnœa and orthopnea The left lung was consolidated The patient died on the fourteenth day Post mortem examination revealed an advanced chronic interstitial nephritis with a *typical secondarily contracted* kidney in an advanced stage

Case No 7—*A B aged* 10 *female* Race mixed Locality Christianburg Demerara river

History was healthy up to 1926 when she contracted fever Since it has attacked her at very frequent intervals

28/4/28 admitted to hospital with fever and œdema of

the feet and face since ten days General state of nutrition good spleen passes the costal margin by 2 inches Marked œdema of the ankles and face Small amount of free fluid in the abdominal cavity anæmic Temperature 100 3 F Blood *P malariæ* (trophozoits and gametes) Stool ova of ascaris present Urine albumin positive 4 per mille sediment hyaline granular and epithelial casts fewleukocytes no red cells Treatment quinine hydrochlor gr 5 t d s theobromin gr 2 t d s mist alba drach 2 mane Diet milk mashed potatoes rice sago Clinical course the temperature fell to normal on the second and third days but again rose to 10° 2 F on the fourth (quartan periodicity) It did not return again

After the fall of the fever the œdema rapidly disappeared and the amount of albumin in the urine fell to 0 5 per mille but was still present when discharged on the twenty fourth day (May 21st 1908)

28/12/08 has taken a series of quinine treatment (gr 5 t d s) at frequent intervals has had two attacks of fever both of which lasted only one day Feels well and considers herself in good health goes to school regularly takes ordinary diet Urine albumin 0 5 per mille sediment shows a few hyaline casts no cells

Case No 8 — A F aged 8 male Race Aboriginal Indian Locality Mari Mari Upper Demerara river

History had a first attack of malaria at the age of one year Was sick during the 1906 epidemic and has suffered from frequent attacks ever since scarcely a month passing without one Each attack lasted from one to five days the paroxysms being preceded by rigors and followed by sweating No other disease or condition worthy of note Since several months the fever attacks have been accompanied by transitory œdema of the face and ankles but the general condition remained fair During this period he was treated on five

occasions by the Government dispenser each course of treatment lasting one week Two weeks previous to admission during an attack of fever general anasarca of high degree made its appearance

5/2/29 admitted to hospital very marked œdema of the face the eyes being partly closed of the feet legs genitals and abdominal wall The abdomen is distended and contains abundant free fluid Temperature 98 F *Weight 53 lb Blood P malariæ (gametes and rings)* Without treatment but only by keeping the patient at rest in bed the parasites disappeared from the peripheral blood on the third day Stool negative Urine amount in twenty four hours 1 100 Albumin positive 5 per mille Urea 0 5 urea concentration test 2 1 per cent diastatic test 6 6 sediment hyaline and granular casts few leukocytes no red cells Treatment quinine gr 5 t d s urea drach ½ t d s mist alba drach 2 mane Diet soft mixed Clinical course improvement was rapid and uninterrupted with the disappearance of œdema the albumin decreased progressively Discharged on the twenty second day weight 38 lbs albumin 0 4 per mille diastatic test 20

CASE NO 9—S F aged 14 female Race Mixed Locality Retreat Upper Demerara river

History began having fever three weeks after birth It lasted for one month Since it has returned with short intervals of one or two weeks Only on one or two occasions she was treated by a dispenser the treatment only lasting for a few days *Œdema appeared two* months before admission at first as a transitory symptom accompanying the fever then as a permanent condition She was treated in Georgetown but with little success

29/12/28 admitted to hospital presents a very marked œdema of the face the eyes are closed the feet legs and

hands are swollen the abdomen is enormously distended with fluid Spleen reaches the navel Temperature normal The patient is very anæmic weak and listless Weight 18 lb 7 oz Blood positive for *P malariæ* very abundant in all developmental stages Stool watery (5 or 6 daily) negative for ova of helminths Urine positive for albumin 8 per mille gr 1 010 sediment hyalin granular and epithelial casts few leukocytes no red cells Diastatic test 10 Treatment quinine gr 3 t d s urea drach ½ t d s Clinical course on account of the intense dyspnœa 1 000 c c of liquid were removed by paracentesis The general condition improved rapidly the weight fell from 15 lbs 7 oz on the sixth day to 10 lbs 6 oz on the sixteenth day the albumin fell to 1 per mille and casts became very scarce in the sediment The patient was discharged in fair general condition with no sign of œdema after sixteen days of treatment

CASE No 10 I C aged 4 Race Portuguese Locality Christianburg Demerara river Shopkeeper

History healthy up to the beginning of 1927

1/8 7 treated as out patient for malaria fever

8 1 7 admitted to hospital for intermittent fever with quartan periodicity of two months standing Since six weeks œdema of the face hands legs genitals and abdominal wall swelling of the abdomen continual headaches and lumbar pain Temperature 102 F Pulse 130 very œdematous very anæmic and weak the spleen passes the costal margin by 4 inches Blood shows very abundant *P malariæ* schizonts and gametes Stool negative Urine albumin positive ? per mille sediment abundant hyalin granular and epithelial casts few leukocytes no red cells Urea concentration test 2 Treatment quinine gr 5 four times daily theobromin gr 4 t d s mist alba oz ½ mane Diet milk Clinical course the fever fell

on the fourth day and with it the œdema began rapidly to decrease The diet was gradually increased and the patient was discharged on the twenty fourth day with normal urine no œdema and feeling well Since he has taken quinine *regularly and has kept in good health while doing his normal work*

CASE NO 11—A A aged 4 male Race Negro Locality Christianburg Demerara river

History suffered from no disease up to the age of two he contracted malaria during the 1926 epidemic

10/11/26 seen as out patient for malaria fever blood not examined

23/11/28 since the last examination the child has suffered from fever on and off The attacks were not severe with a tertian periodicity During the last two months the *fever has been nearly continuous with the same periodicity* accompanied by very profuse sweating and abdominal pain Slight œdema The general state of nutrition is poor the spleen is palpable at the costal margin Blood positive for *P malariæ* trophozoits and gametes very abundant Stool positive for ova of trichuris Urine positive for albumin ½ per mille sediment shows abundant hyalin and granular casts very few leukocytes no red cells Treatment quinine gr 3 t d s for two weeks theobromin gr 1½ t d s for ten days Diet milk

3/12/28 has had no fever since last examination and *appears in good health The urine contains a trace of* albumin the sediment contains very few hyalin and granular casts Above treatment repeated

22/3/29 seen again as out patient contrarily to advice the mother has interrupted treatment for the last two months Two weeks ago the fever again made its appearance The spleen is well palpable at the costal margin there is no œdema Blood shows numerous *P malariæ* bands and

gametes Urine albumin positive ½ per mille sediment negative

CASE No 12—G C aged 13 male Race mixed Locality Bootoba Demerara river

History has had very little fever up to three years ago contracted malaria in 1927 since scarcely a month has passed without one or more attacks of fever In May 1928 he developed œdema of the feet and face and a swelling of the abdomen after an attack of fever These symptoms subsided after a few weeks and have not returned since in spite of repeated attacks of fever

18/5/29 has suffered from fever for the last two weeks every other day with ague Suffers much with headache admitted to hospital General condition of nutrition fair very anæmic the spleen reaches the umbilical line there is no œdema Blood positive for *P malariæ* (trophozoits) Stool shows ova of *Ancylostoma Ascaris* and *Trichuris* Meinicke and Hecht reactions negative Urine albumin positive 4 per mille sediment abundant hyalin and granular casts Urea concentration test 1 4 diastatic test 10

CASE No 13—A S age 8 years and 5 months male Race mixed Locality Maria Elizabeth Demerara river

History has suffered from fever from the age of seventeen months Was treated for malaria in October 1926

7/10/26 seen as out patient for fever general state of nutrition poor the spleen reaches the umbilical line and is hard and tender Blood negative Has repeatedly been treated as out patient since at the Akyma dispensary

24/11/28 seen as out patient The mother states that he has suffered from intermittent fever since two years at very frequent intervals since one month œdema of the

face and feet and swelling of the abdomen have appeared General condition of nutrition very poor the spleen is very hard and reaches the umbilical line There is slight œdema of the feet while on the face abdominal wall and genitals it is very marked The abdomen is distended and contains a large amount of free fluid Temperature 98 4 F Blood shows a heavy infection with *P malariæ* with parasites in all developmental stages Anisocytosis and poikilocytosis Basophilic red cells Stool negative Urine albumin positive 5 per mille The sediment shows a large number of hyalin granular and epithelial casts few leukocytes and no red cells Treatment quinine gr 3 t d s for twenty days theobromin gr 1½ t d s cod liver oil drach 1 t d s

CASE No 14—C W aged 5 female Race mixed Locality Seba Demerara river

History the child was healthy up to the end of 1926 when she contracted malaria during the epidemic She has suffered from fever at very frequent intervals ever since each attack lasting for three or four days with quotidian periodicity often preceded by rigors and followed by sweating *She has only been treated on four occasions by a* dispenser each course of treatment lasting approximately one week

22/2/29 admitted to hospital for fever which started two weeks ago accompanied by œdema of the face and legs this condition lasted for three days disappearing with the fever As soon as the child got up again the fever returned and with it the œdema General condition of nutrition fair Spleen not palpable Very marked generalised œdema. The abdomen is distended containing a large amount of free fluid Weight 39 lbs 6 oz Temperature 101 F Pulse 120 Blood shows a heavy infection with *P malariæ* (trophozoits) Stool negative for ova of helminths

Urine positive for albumin 9 per mille sp gr 1 014 reaction acid amount passed in twenty four hours 1 000 c c urea 1 5 per cent sediment hyaline and granular casts urea concentration test 1 5 diastatic test 6 6 Treatment quinine gr 4 t d s theobromine gr $1\frac{1}{2}$ t d s cod liver-oil gr 2 t d s Diet milk Clinical course the temperature showed a slight quotidian elevation to 99 and 99 4 F for the following three days it then fell to normal the œdema falling progressively and rapidly the weight of 39 lbs 6 oz on admission fell to 36 lbs on the fifth day and 34 lbs on the ninth The amount of urine passed in the twenty four hours did not show much variation averaging 1 000 c c The amount of albumin decreased rapidly to 4 per mille while the urea concentration test and the diastatic test rose to 1 8 and 10 respectively (March 3rd 19 9) The patient was dismissed on March 4th 19 9 with recommendation to continue the same treatment for one month without diet restrictions

0/3 9 reports to have had no fever since her discharge and to be feeling well looks well spleen reduced to the costal margin Urine albumin positive 4 9 per mille sediment very few hyaline and granular casts no cells diastatic test 10

CASE No 15 —W K aged 30 male Race Negro Locality Mackenzie Demerara river Mechanic

History has been under observation as a labourer for seven years During this period the only disease for which he received treatment was malaria fever and this only since the beginning of 19-7

7/3/27 admitted to hospital for malaria fever

15/5/27 treated as out patient for chronic malaria

-/4/28 admitted to hospital for malaria fever Urine normal

2 /9/28 seen as out patient for fever lumbar pain and

slight œdema of the ankles Blood not examined urine contains a trace of albumin

17/2/29 admitted to hospital with generalised œdema of the face feet abdominal wall and genitals and peritoneal effusion he states that these symptoms came on with fever during the last four days He admits to have suffered from low fever for many months but did not attribute much importance to it as it did not interfere with his work it came on particularly at night Temperature 98 1 F Pulse 80 General state of nutrition good spleen not palpable anæmic Weight 179 lbs Blood positive for *P malariæ* (trophozoits) Stool positive for ova of ankylostoma Meinicke and Hecht reactions negative Widal reaction with T A B C emulsions negative Urine amount passed in twenty four hours 110 c c Positive for albumin 15 per mille sp gr 1 010 urea concentration test 1 5 diastatic test 6 6 sediment abundant granular hyaline and epithelial casts few leukocytes no red cells Blood pressure systolic 150 mm diastolic 90 differential 60 mm Treatment quinine gr 10 t d s urea drach 2 t d s On the twenty fifth day carbon tetrachloride M 35 Diet milk Clinical course the temperature remained normal throughout Polyuria set in from the third day with the passage of from 2 500 to 5 000 c c of clear urine per day The œdema and peritoneal effusion rapidly reduced and at the end of the first week the weight had fallen by 16 lbs and by 31 lbs on the thirty ninth day when the patient was discharged The albumin had fallen to 2 per mille

6/4/29 feeling well albumin 1 9 per mille urea concentration 2 5 diastatic test 20

19/5/29 has been working since four weeks Has had no more fever and no œdema Albumin 6 per mille sediment very few hyaline casts

CASE No 16 — E F aged 7 male Race Aboriginal Indian Locality Mari Mari Upper Demerara river

History was in good health up to the age of five He contracted malaria at the end of 1906 Since he has had continual attacks of intermittent fever with scarcely a week



FIG 15



FIG 16

FIG 15 and 16 — Chronic Nephritis in a male Aboriginal Indian aged seven years suffering from chronic B T Malaria for over two years

or ten days in between The fever was accompanied with pain in the splenic region and frequently preceded by rigors and followed by sweating sometimes bilious vomiting occurred He never had blackwater

18/1/09 admitted to hospital complaining of fever for

the past three weeks and œdema of the face and feet and swelling of the abdomen since one week The eyes are nearly closed and the scrotum and prepuce highly distended (Figs 15 and 16) The spleen reaches the umbilical line Temperature 101 F Weight 53 lbs Blood shows a heavy double infection with *P vivax* and *P malariæ* the latter in all developmental stages Stool shows large numbers of ova of *Ascaris* and a few of *Ancylostoma* Meinicke and Hecht reactions negative Widal reaction with T A B C emulsions negative Urine amount passed in twenty four hours 500 c c gr 1 012 reaction acid albumin positive 8 per mille urea concentration test 1 6 diastatic test 6 6 Treatment was commenced on the eleventh day quinine gr 5 t d s urea drach 1 t d s Ol chenopodii M 3 for three consecutive doses Diet soft mixed Clinical course no treatment was administered for the first ten days the fever fell on the fourth day but parasites of the quartan variety remained very abundant in the peripheral blood while the general condition remained stationary With the institution of the above treatment immediate response was noted the œdema reduced with a rapid fall in the weight while the amount of urine passed in twenty four hours was trebled the amount of albumin showed a similar fall Following the anti helminthic treatment the patient passed nine ascarids The patient was discharged on February 12th 1929 (twenty fifth day) being provided with treatment for one month a above All trace of œdema had disappeared The spleen could be just felt at the costal margin and the weight had fallen to 48 lbs The amount of urine passed in twenty four hours was 1 500 c c Albumin was still present 1 per mille the sediment showed only a few hyaline casts urea concentration test 1 5 diastatic test 10

Chronic Benign Tertian Malarial Fever Chronic Nephritis

CASE No 17—E A aged 10 female Race mixed Locality Christianburg Demerara river (sister of case No 5)

History healthy infancy with only rare attacks of fever contracted malaria in 1926 and has suffered at frequent intervals ever since

6/?/ 8 admitted to hospital with a history of fever since ten days with generalised œdema and ascites General condition of nutrition fair weak Temperature 101 F Pulse 144 Face legs and genitals very œdematous abdomen highly distended containing free fluid Blood shows a heavy infection with large rings returned as *P viv ax* Stool negative for ova of helminthes Urine amount passed in twenty four hours 0.0 c c gr 1 010 albumin positive 7 per mille sediment hyaline granular and epithelial casts few leukocytes no red cells Treatment quinine gr 5 t d s urea drach 4 t d s mist alba drach 1 mane Diet milk Clinical course the temperature fell to normal on the second day on the fourth day there was a slight rise to 99 F (quartan?) After the fall of the temperature the œdema rapidly reduced and disappeared the patient was discharged on the eleventh day with treatment for three weeks and recommendation to continue it over a period of three months

8/3/ 8 the patient reports to be feeling well has had no fever or œdema since her discharge from hospital

8 12 8 since last examination she has had fever twice but no œdema she has taken quinine regularly with occasional intervals and has used full ordinary diet she feels and looks well albumin positive 1.5 per cent sediment few hyaline and granular casts present no white or red cells

the past three weeks and œdema of the face and feet and swelling of the abdomen since one week The eyes are nearly closed and the scrotum and prepuce highly distended (Figs 15 and 16) The spleen reaches the umbilical line *Temperature* 101 F *Weight* 53 lbs *Blood* shows a heavy double infection with *P vivax* and *P malariæ* the latter in all developmental stages Stool shows large numbers of ova of *Ascaris* and a few of *Ancylostoma* Meinicke and Hecht reactions negative Widal reaction with T A B C emulsions negative Urine amount passed in twenty four hours 500 c c gr 1 012 reaction acid albumin positive 8 per mille urea concentration test 1 6 diastatic test 6 6 Treatment was commenced on the eleventh day quinine gr 5 t d s urea drach 1 t d s Ol chenopodii M 3 for three consecutive doses Diet soft mixed Clinical course no treatment was administered for the first ten days the fever fell on the fourth day but parasites of the quartan variety remained very abundant in the peripheral blood while the general condition remained stationary With the institution of the above treatment immediate response was noted the œdema reduced with a rapid fall in the weight while the amount of urine passed in twenty four hours was trebled the amount of albumin showed a similar fall Following the anti helminthic treat ment the patient passed nine ascarids The patient was discharged on February 12th 1929 (twenty fifth day) being provided with treatment for one month a above All trace of œdema had disappeared The spleen could be just felt at the costal margin and the weight had fallen to 43 lbs The amount of urine passed in twenty four hours was 1 500 c c Albumin was still present 1 per mille the sediment showed only a few hyaline casts urea concentration test 1 5 diastatic test 10

Chronic Benign Tertian Malarial Fever Chronic Nephritis

CASE No 17 —E A aged 10 female Race mixed Locality Christianburg Demerara river (sister of case No 5)

History healthy infancy with only rare attacks of fever contracted malaria in 1926 and has suffered at frequent intervals ever since

6/2/28 admitted to hospital with a history of fever since ten days with generalised œdema and ascites General condition of nutrition fair weak Temperature 101 F Pulse 144 Face legs and genitals very œdematous abdomen highly distended containing free fluid Blood shows a heavy infection with large rings returned as *P vivax* Stool negative for ova of helminthes Urine amount passed in twenty four hours 950 c c gr 1 010 albumin positive 7 per mille sediment hyaline granular and epithelial casts few leukocytes no red cells Treatment quinine gr 5 t d s urea drach ½ t d s mist alba drach 1 mane Diet milk Clinical course the temperature fell to normal on the second day on the fourth day there was a slight rise to 99 F (quartan ?) After the fall of the temperature the œdema rapidly reduced and disappeared the patient was discharged on the eleventh day with treatment for three weeks and recommendation to continue it over a period of three months

8/3/28 the patient reports to be feeling well has had no fever or œdema since her discharge from hospital

28/1 ? 28 since last examination she has had fever twice but no œdema she has taken quinine regularly with occasional intervals and has used full ordinary diet she feels and looks well albumin positive 1 5 per cent sediment few hyaline and granular casts present no white or red cells

CASE NO 18 —D A aged 2 years and 9 months female Race mixed Locality Old England Demerara river

5/2/27 seen as out patient aged eleven months suffering from fever *since four days with diarrhœa and vomiting* Spleen palpable at the costal margin very anæmic Enteric suspected warned to return in two days for further examination Quinine gr 3 t d s prescribed provisionally

7/2/27 admitted to hospital condition stationary temperature 103 F Blood negative for malaria parasites marked anisocytosis and poikilocytosis with numerous basophilic red cells Hæmoculture positive for *Bact paratyphosum C* Discharged convalescing on the fifteenth day

19/6/28 seen as out patient fever since two weeks spleen enlarged and tender œdema of the face feet and abdominal wall Blood positive for large ring forms returned as *P vivax* Urine albumin trace sediment negative Treatment quinine hydrochlor gr 8 t d s for twenty days (to be repeated) mist alba drach 1 mane

24/11/28 seen as out patient for intermittent fever lasting since ten days with vomiting and œdema Marked swelling of the feet and face the peritoneal cavity contains a considerable amount of free fluid the spleen reaches to the umbilical line Blood shows numerous *P vivax* trophozoits and gametes Stool negative Urine albumin positive 1 per *mille sediment hyaline and granular casts* very abundant Treatment as above

3/1/29 returns with a history of fever since five days having stopped the treatment three weeks previously she presents slight œdema of the face and ankles Blood *P vivax* trophozoits and rings abundant Urine positive for albumin 1 per mille Treatment as above with cod liver oil drach 1 t d s

22/1/29 Blood negative Urine albumin 1 9 per mille sediment contains abundant casts few leukocytes and no red cells Treatment as above

31/3/29 seen as out patient with a history of fever since

four days marked œdema of the face and feet The treat ment had been stopped since one month Blood negative Urine albumin positive 4 5 per mille

CASE No 19 —T S aged 24 male Race Negro Native of Grenada B W I Miner

History enjoyed good health while in Grenada and only suffered from fever on rare occasions Denies having had yaws Came to Demerara six months ago and has worked since as woodcutter at Akyma Demerara river Two weeks after his arrival he had an attack of fever with rigors ague and sweating Since he has suffered continually with repeated attacks usually brought on by exposure while at work. One month ago during an attack of fever he noted œdema of the ankles and of the face which lasted for four days

28/8/28 seen as out patient complaining of fever for the last three weeks with œdema of the ankles Blood positive for large ring forms returned as *P vivax* Urine albumin positive 0 2 per mille sediment granular and hyaline casts no cells Blood pressure systolic 110 mm diastolic 60 mm differential 50 mm Treatment quinine gr 12 b d s for fifteen days

22/10/28 reports to have suffered repeatedly from fever since last examination complains of debility and dyspnœa very anæmic spleen not palpable

7/12/28 re examined no œdema anæmic spleen not palpable Blood positive for large ring forms Meinicke and Hecht reactions negative Widal reaction with T A B C emulsions negative Urine positive for albumin 0 2 per mille sediment shows few hyaline and granular casts and few leukocytes

CASE No 20 —E F aged 19 male Race Mixed Locality Bootooba Demerara river Woodcutter

History the patient states to have only rarely suffered from fever before the epidemic He contracted malaria in December 1926 and has been subject to recurrent attacks at short intervals ever since The attacks are characterised by sharp fever paroxysms accompanied by rigors and sometimes followed by sweating the spleen became larger and more painful He never had blackwater Since ten days with an attack of fever œdema of the legs and abdominal wall has set in Even slight exertion is rendered difficult by dyspnœa

5/10/28 admitted to hospital *Temperature* 99 2 F subicteric tinge of the scleræ and skin marked œdema of the legs genitals abdominal wall and face free fluid in the abdomen the spleen reaches to the navel the liver is in its normal limits Blood *P vivax* rings Stool hook worm ova present Meinicke and Hecht reactions negative Blood pressure systolic 140 mm diastolic 90 mm differential 50 mm Urine positive for albumin 6 per mille sediment hyaline epithelial and granular casts few leukocytes no red cells urea concentration test 2 Treatment quinine gr 10 t d s theobromine gr 4 t d s carbon tetrachloride 35 M mag sulph ½ oz Diet soft mixed Clinical course 344 hook worms were passed on the day following the administration of carbon tetrachloride From the fifth day a course of iron and arsenic injections was instituted The patient was discharged much improved on the eighteenth day feeling well

27/11/28 *took quinine regularly up to one week ago* Fever returned after three days no œdema feels well Blood *P vivax* rings Urine albumin 1 per mille Treatment quinine hydrochlor gr 10 daily for one month

25/2/29 reports to have been working (timber squaring) for the last two months Has had no fever but occasionally slight œdema of the feet Spleen very large filling the whole left side of the abdomen to the pubis Urine albumin 0 4 per mille no sediment

CASE No 21 —V M aged 26 male Race Negro Locality native of Grenada B W I residing at Akyma Demerara river Miner

History in his native island he only once suffered from fever for two weeks with a cold He had a sore of the left leg which was treated with two intravenous injections he had yaws as a child He came to Demerara in June 19?6

10/7/?6 physically examined for employment returned as fit with normal urine

3/1/?7 admitted to hospital with a history of fever he had his first attack in August 1?26 Blood negative (has taken quinine) for malaria parasites positive for *Micro filaria bancrofti* Stool positive for ova of *Ascaris* Urine negative for albumin With quinine treatment the fever fell to normal on the second day

7/ /?7 admitted with a history of fever since one week Blood negative Urine positive for albumin trace

30/7/ ? admitted with a history of fever every day since two weeks with headache rigors and nausea œdema of the face and ankles swelling of the abdomen and diminution of vision Blood *P vivax* present with abundant ring forms Urine positive for albumin 2 per mille sediment hyaline and granular casts few leukocytes no red cells urea concentration test 0 6

8/11/?8 admitted with a history of fever every other day and a large painful spleen no œdema Blood *P vivax* rings present Urine albumin positive 3 per mille

3/11/28 re examined has had no more fever Urine albumin positive 5 per mille leukocytes hyaline granular and epithelial casts very abundant Blood pressure systolic 120 mm diastolic 85 mm differential 3? mm

CASE No ?? —D F aged ? female Race mixed Locality Bootooba Demerara river

History was in good health up to the age of twenty Contracted malaria during the 1926 epidemic and has suffered from very frequent recurrences ever since Two months ago during an attack of fever, œdema of the face and ankles appeared This condition has gradually progressed with alternatives of increase and reduction in relation to the incidence of fever attacks She has had fever ague and vomiting for the last two weeks

1/3/28 admitted to hospital general state of nutrition fair weak *anæmic enormously hydropic with huge* œdema of the legs and large peritoneal effusion Marked dyspnœa *and orthopnea* The *spleen reaches the umbilical* line Bowels loose with six or seven watery stools daily Temperature normal Pulse 100 Blood pressure *systolic 140 diastolic 110* differential *30 mm Blood P vivax* trophozoits very numerous Stool negative Urine amount passed in twenty four hours 600 c c albumin positive 2 per mille sediment abundant granular hyaline and epithelial casts few leukocytes no red cells urea concentration test 1 5 Treatment quinine hydrochlor gr 5 four times daily theobromin gr 4 t d s mist alba oz ½ mane Clinical course the condition remained practically stationary for two weeks Then progress became rapid the œdema reduced and disappeared parallel to the reducing of the spleen The patient was discharged on the fifty eighth day all trace of œdema having disappeared and the spleen being reduced to the costal margin She was given treatment for one month and advised to continue *to take quinine in gr 10 doses daily for six months*

8/11/28 seen as out patient looks very well has been taking quinine as prescribed with short intervals as the drug is not always procurable on the *upper course of the river* Has had fever during the past few days dropsical symptoms have never recurred since her discharge She has been working hard for the past eight months *without effort or* consequences Blood positive for *P vivax* rings Urine

positive for albumin ½ per mille sediment very few hyaline casts no cells Blood pressure systolic 140 diastolic 110 differential 30 mm

CASE No 93—R P aged 23 male Race Negro Native of Georgetown resident at Akyma Demerara river since seven years Miner Did not suffer from any particular disease while in Georgetown

June 1923 physically examined for employment returned as fit urine normal

21/6/27 treated as out patient for fever

21/7/27 treated as out patient for a ting ting spider (*Latrodectes*) bite

2/10/28 again examined for employment returned as fit urine normal

15/1/29 admitted to hospital for fever dating since three days Temperature 101 F Spleen not palpable no oedema Blood positive for *P vivax* ring forms Stool positive for ova of ankylostoma Meinicke and Hecht reactions negative Urine amount passed in twenty four hours 950 c c sp gr 1 014 reaction acid Albumin positive 1 per mille sediment hyaline granular and epithelial casts few white cells urea concentration test 2 5 diastatic test 10 Treatment quinine gr 10 t d s Diet soft mixed Clinical course the amount of albumin in the urine decreased considerably falling to 0 2 per mille after one week The patient was discharged on January 25th 1929 with the same treatment as above for one month

11/2/29 re examined feels quite fit Urine contains 0 9 per mille of albumin the sediment shows very few hyaline casts

CASE No 94—C P aged 2. male Race Negro

Native of Georgetown residing in Mackenzie Demerara river since October 1927 Carpenter

History enjoyed good health while in Georgetown being a boxer of some repute

17/10/27 physically examined for employment returned as fit urine normal

13/12/27 admitted to hospital for fever with vomiting and dizziness Blood negative urine normal

24/5/28 admitted to hospital for fever with tertian periodicity Blood positive for *P vivax* urine normal

17/7/28 seen as out patient for malaria fever

4/9/28 seen as out patient for fever lasting since two days with œdema of the face and feet Blood positive for *P vivax* ring forms Urine positive for albumin 1 per mille sediment contains hyaline granular and epithelial casts few leukocytes no red cells urea concentration test 2 Treatment quinine gr 10 t d s theobromine gr 4 t d s Diet soft mixed Discharged on the tenth day the œdema having disappeared but with a trace of albumin still present in the urine

20/12/28 admitted to hospital for fever with œdema of the face and feet dating since one week. General state of nutrition good slightly anæmic there is very considerable œdema of the feet legs abdominal wall and face free fluid *is present in the abdomen and the patient appears markedly* dyspnœic on exertion Blood pressure systolic 110 diastolic 70 differential 40 mm Blood positive for *P vivax* ring forms Stool positive for ova of *Ancylostoma* Meinicke and Hecht reactions negative Widal test with T A B C emulsions negative Urine amount passed in twenty four hours 1 650 c c sp gr 1 010 reaction acid Albumin positive 4 5 per mille sediment hyaline granular and epithelial casts numerous leukocytes no red cells urea concentration test 0 7 diastatic test 20 Treatment *quinine gr 10 t d s Diet soft mixed* Clinical course the patient remained in hospital thirty days though the

general state improved rapidly with the fall of the fever and the disappearance of the œdema the urine remained albuminous the amount being reduced to 1 per mille

?6/ /?9 the patient has returned to work (carpenter) since twenty six days and feels well The amount of albumin has increased to 6 per mille

18/3/29 admitted to hospital for numerous venereal chancres of the prepuce and a bubo in the left groin Urine contains 4 per mille of albumin Treatment quinine gr 10 t d s Streptobacillary vaccine by intravenous injection on alternate days Discharged on the tenth day the bubo reabsorbing and the chancre healed albuminuria 3 per mille

15/4/2? re examined albuminuria fallen to ? per mille sediment very scarce working feeling well

CASE No ?—V B aged 2 female Race mixed Locality Mahaicaballi Demerara river

Had a first attack of fever at the a e of seven days in November 19?6 she has since suffered constantly hardly a month passing without an attack she never had œdema She was treated at our hospital and dispensaries repeatedly for fever the disease always being interrupted by quinine treatment

13/12/ 8 very anæmic the spleen passes the costal margin by inches has had fever since five days with chills and sweats Blood positive for *P vivax* rings Urine albumin positive 0 per mille sediment abundant hyaline and granular casts and white cells

? /1 / 8 no fever doing well Urine albumin 0 5 per mille sediment very few granular casts Treatment quinine gr 3 t d s

9/1/?? stopped treatment one week ago the fever has relapsed since yesterday Blood positive for *P vivax* albuminuria 1 per mille

CASE No 26—A N aged 19 female Race mixed Locality Akyma Demerara river

History has had fever off and on at frequent intervals since 1926

20/11/28 seen as out patient for quotidian intermittent fever lasting since two weeks with headache splenomegaly lumbar pain rigors sweats and bilious vomiting Œdema of the face in the morning Temperature 99 F Blood positive for *P vivax* ring forms Stool positive for ova of *Ancylostoma* and for larvæ of strongyloides Treatment quinine gr 5 t d s theobromine gr 4 t d s Diet mixed

29/11/28 still getting fever and feeling weak admitted to hospital Blood negative for malaria parasites marked anisocytosis and numerous basophilic red cells Meinicke and Hecht reactions negative Widal reaction with T A B C emulsions negative Urine amount passed in twenty four hours 800 c c albumin present 1 per mille urea concentration test 0 8 sediment hyaline and granular casts

7/12/28 re examined states to be feeling well urine albuminuria 0 5 per mille granular and hyaline casts

22/12/28 re examined has taken quinine regularly feels and looks well Has had no more fever or œdema Urine albumin present 1 per mille the sediment contains few hyaline casts

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